EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 8
372-376
Year: 2020

CORRELATION OF CYTOLOGY, COLPOSCOPY WITH HISTOPATHOLOGY DURING OPPORTUNISTIC SCREENING FOR CERVICAL PRECANCER LESIONS

Dr. Shazia Anjum[1], Dr. Vandana Saini*[2] and Dr. Mamta Gupta[3]

[2]Senior Specialist, Department of Obstetrics and Gynaecology, Hindu Rao Hospital and Associated NDMC Medical College, Delhi, India.
[1]Post Graduate Candidate, Department of Obstetrics and Gynaecology, Hindu Rao Hospital and Associated NDMC Medical College, Delhi, India.
[3]Senior Consultant, ex-HOD, Department of Obstetrics and Gynaecology, Hindu Rao Hospital and Associated NDMC Medical College, Delhi, India.

***Corresponding Author: Dr. Vandana Saini**
Post Graduate Candidate, Department of Obstetrics and Gynaecology, Hindu Rao Hospital and associated NDMC Medical College, Delhi, India.

Article Received on 27/05/2020 **Article Revised on 18/06/2020** **Article Accepted on 09/07/2020**

ABSTRACT

Background: Cervical cancer is second most common cancer in women in India. It is a preventable disease as it has a well-defined long premalignant phase that can be detected by regular screening tests and follow up. **Aim and Objective:** The aim of this study was to compare detection of the premalignant lesions of cervix by Pap smear, colposcopy and cervical biopsy in women with gynecological complaints. **Materials and Methods:** This cross-sectional study was conducted on 100 women who attended Gynaecology OPD with gynecological complaints in June 2018. In the Department of Obstetrics and Gynae at Hindu Rao, Hospital and associated NDMC Medical College, Delhi. All women had Pap smear test by conventional method and colposcopy done at their 1st visit. Women with abnormal colposcopy findings were subjected to cervical biopsy. The results of Pap smear and colposcopy were analyzed and correlated with cervical biopsy. **Results:** The sensitivity of Pap smear was 45.00%, specificity 60.00%, positive predictive value 69.23%, negative predictive value 35.29% and an accuracy rate of 50.00% for detecting pre-malignant and malignant lesions of cervix. Colposcopy had much higher sensitivity (100%), positive predictive value 74.07%, with accuracy of 76.67% and negative predictive value 100% but had a lower specificity of 30.00%. **Conclusion:** Pap smear had poor sensitivity compared to colposcopy. Colposcopy had high sensitivity and higher accuracy though the specificity rate was less compared to Pap smear test. Hence, it is suggested that both the tests should be utilized for screening of premalignant lesions of cervix.

KEYWORDS: Pap smear, colposcopy, histopathology, colposcopically directed biopsy, Lugols Iodine.

INTRODUCTION

Cervical cancer is the 4th most common cancer in women and represents 6.6% of all female cancers globally as per WHO report.[1] India accounts for 1/4th of global burden of cervical cancer according to a report prepared by NICPR.[2] An estimated 30,000 new cases of cervical cancer and 73,000 deaths in 2008 and 96,922 new cases and 60,078 deaths have been reported in India during 2018.[3] It is responsible for 20% of all female deaths[4] where every 8 minute a woman dies due to cervical cancer.[5] This cancer is among the most preventable cancers because of its slow progression providing ample time for screening, the presence of detectable lesions using cytology, and the introduction of preventive therapy and effective treatments if detected in early stage.[6]

Pap test is a cytodiagnostic study of spontaneously exfoliated or mechanically dislodged cells (surface microbiopsy) of cervix for detection of pre-cancerous and cancerous lesions. It has been the most widely prevalent test for screening cervical cancer, one of the easily preventable forms of cancer in the women. Colposcopy is direct examination of cervix under magnification. Acetic acid coagulates the nuclear proteins and stromal cytokeratins of the dysplastic cells which can be visualized as acetowhite areas.[7] Lugols iodine stains the healthy squamous cells brown and not the dysplastic cells.[8] These iodine negative areas can also be visualized by colposcope.

The accessibility of the cervix to cytological testing by Pap testing, is a simple OPD procedure. However, the sensitivity of Pap smear is quite low (40-65%).[9,10] though its specificity remains high (80-95%).[10,11] Thus the pickup rate of pre-cervical cancer is poor using pap

test alone, and many cases are therefore missed. It seems imperative to improve the sensitivity of Pap test by complementing with a simple OPD procedure. Hence, in this study, we have made use of the Pap smear test along with colposcopy as a composite screening procedure to evaluate whether addition of colposcopy can improve sensitivity to pick up pre-malignant cervical lesions.

METHODOLOGY

This cross sectional study was conducted in the Department of Obstetrics & Gynaecology Hindu Rao Hospital, New Delhi. One hundred women attending Gynae OPD were enrolled after written consent, who fulfilled the inclusion criteria i.e. women with age 21-65 years, sexually active with one of the complaints - persistent leucorrhoea, post coital bleeding, postmenopausal bleeding, foul smelling vaginal discharge and / or unhealthy looking cervix on speculum examination. Women with diagnosed cervical cancer, who had undergone hysterectomy, pregnant and postpartum women, unmarried women, who did not gave consent for participation in the study were excluded from the study.

Ethical committee of the institute approved the study. A detailed history was taken including age, age at first sexual intercourse, menstrual history, number of conceptions, inter pregnancy interval, history of sexual intercourse with multiple partners etc. General and systemic examination was done. Speculum examination of cervix was done to see for any vaginal/cervical discharge, ectropion, polyp, nabothian follicle, inflammation, condylomata, ulcer, growth or any lesions in the cervix and vagina. All women were subjected to Pap smear for cytology from ecto and endo cervix using Ayer's spatula and endocervical sampling brush. Colposcopy was done in the same sitting. Site of the abnormal areas was recorded. Women with abnormal colposcopic findings underwent cervical biopsy.

Pap smear was reported according to the Modified Bethesda System.[12] Cytology of ASC-US (atypical squamous cells), ASC-H (cannot exclude HSIL), LSIL (low grade squamous intraepithelial lesion), HSIL (high grade squamous intraepithelial lesion) and SCC (high grade squamous intraepithelial lesion) were taken as Pap smear positive.

For colposcopy, excess mucus was removed from the cervix with saline soaked cotton swabs. Cervix was visualized using auto-focusing and digital magnification (x 5-20). Abnormal looking areas were identified. Green filter was used to see abnormal vessels. Five percent acetic acid was then applied to cervix to see for any acetowhite area, its margins, contour, intensity were recorded. Lugol's iodine was then applied over cervix using cotton swab. Iodine uptake was noted as brown (positive uptake), yellow-brown (partial uptake) and areas of no uptake (negative uptake).

Colposcopic findings were scored and recorded as per modified Reids scoring index.[13] Abnormal epithelium was considered with a Reid's score of more than 2. Cervical biopsy was taken from acetowhite area and Lugols negative area with Reids score >2.

All the data was recorded in a pre-designed proforma and analyzed. P value of less than 0.05 was considered significant.

RESULTS

Table 1: Demographic distribution of cases.

Parameter		n (%)	Intraepithelial lesions detected	p value
Age in years (n=100)	<30	7	0	0.384
	31-60	89	19	
	>60	4	1	
Parity (n=100)	<3	36	4	0.121
	≥3	64	16	
Education status (n=100)	Illiterate	45	12	0.209
	Literate	55	8	
Age at first sexual Relation (n=100)	12-15	2	1	0.283
	16-20	56	14	
	21-25	41	5	
	26-30	1	0	

Table 2: Clinical details.

S. No.	Clinical Details	
Gynaecological complaints (n=100)		**N**
1.	Discharge per vaginum	36
2.	Discharge PV with pain in lower abdomen	22
3.	AUB	10
4.	Post coital bleeding	11
5.	Pain and heaviness in lower abdomen	5
6.	Infertility	5
7.	Intermenstrual bleeding	6
8.	Postmenopausal bleeding	5
Speculum Examination Findings (N*=114)		
1.	Healthy cervix	36
2.	Cervical erosion	22
3.	Vaginal discharge	21
4.	Cervical discharge	7
5.	Nabothian follicles	11
6.	Cervicitis	11
7.	Polyp	5
8.	Cervical growth	1

*Some women had more than 1 finding, hence the discrepancy

Table 3: Detection of pre-malignant changes in cervix.

Screening method	Screening details	Report details	N
Pap smear (N=100)	Pap negative (n=87)	NILM	75
		Inflammation	12
	Pap positive (n=13)	ASC-US	9
		ASC-H	1
		LSIL	3
		HSIL	0
Colposcopy Reids index (N=100)	Colpo negative (n=73)	0-2	73
	Colpo positive (n=27)	3-4	13
		5-8	14
Biopsy & Histopathology (N=30)	Biopsy negative (n=10)	Inflammatory	10
	Biopsy positive (n=20)	CIN I	9
		CIN II	7
		CIN III	3
		SCC	1

Table 4: Association between Biopsy and Pap Smear.

Pap smear details	Cervical Biopsy (N=30)				
	Biopsy –ve (n=10)	Biopsy + ve (n=20)			
	Inflammatory	CIN I	CIN II	CIN III	SCC
Negative (N=17)					
NILM (n=15)	6	5	3	1	0
Inflammation (n=2)	0	2	0	0	0
Positive (N=13)					
ASC-US (n=9)	3	1	4	1	0
ASC- H (n=1)	0	0	0	0	1
LSIL (n=3)	1	1	0	1	0
Total	10	9	7	3	1

P value = 0.001(significant)

Table 5: Association between Biopsy and Colposcopy.

Colposcopy Reids score	Cervical biopsy (n=30)				
	Biopsy –ve (n=10)	Biopsy +ve (n=20)			
	Inflammatory	CIN I	CIN II	CIN III	S CC
Negative (N=3) 0-2 (n=3)	3	0	0	0	0
Positive (27) 3-4 (n=13) 5-8 (n=14)	7 0	5 4	1 6	0 3	0 1
Total	10	9	7	3	1

P value=0.009 (significant)

Table 6: Comparison of sensitivity, specificity and accuracy.

Parameter	Pap smear	Colposcopy
Sensitivity	45%	100%
Specificity	60%	30%
NPV	35.29%	100%
PPV	69.23%	74.07%
Accuracy	50%	76.67%

DISCUSSION

In this study we found a prevalence rate of pre-malignant lesions of cervix to be 20% in opportunistic screening in women attending Gynae OPD at our institute with gynecological complaints. This appears to be quite high compared to other studies who have quoted a prevalence rate of only 3% - 5%.[14] This might be because of many referred patients attend our tertiary level institute. All these women require follow up and appropriate treatment, though follow up and treatment was not part of our study.

The mean age of women, in our study was 45.33 years and mean parity 3.04. Age of women, parity, literacy and age at 1st sexual exposure were not associated with abnormal cervical biopsy (p value 0.384, 0.121, 0.209, 0.283 respectively) (Table 1).

The most common gynecological complaint in our study was discharge per vaginum (n=36), followed by discharge per vaginum with pain in lower abdomen (n=22), AUB (n=15), postcoital bleeding (n=6), heaviness in lower abdomen (n=5), infertility (n=5), intermenstrual bleeding (n=6), postmenopausal bleeding (n=5) (Table 2). Cervix was found to be healthy in only 36 women. Unhealthy cervix included cervical erosion (n= 22), vaginal and cervical discharge (n=28), nabothian follicle (n= 11), cervicitis (n=11), polyp (n=5), growth (n=1) (Table 2).

In 100 women who were subjected to pap smear test, we found that only 13 women had premalignant/malignant lesions (Table 3), though the biopsy report confirmed it in only 9 women (2,4,2,1 women with CIN I,II,III and SCC respectively) (Table 4). The sensitivity, specificity, PPV, NPV of Pap test was found to be 45.00%, 60.00%, 69.23%, 35.29% respectively (Table 6). Our results were in corroboration with Garg R et al.[9] who has reported sensitivity of pap smear as 44.04%. Ashmita et al.[13] has reported quite low sensitivity of only 19.5%. However, a high Pap smear sensitivity of 69.25% and 65.38% respectively was reported by Gandi et al, Joshi et al.[10.11] We found specificity of pap smear to be 60% (Table 6), which was quite low than other studies who have reported it be about 83%.[11,13]

We performed colposcopy at the same time in all these 100 women and found 27 women with abnormal colposcopy findings (Table 3). Biopsy confirmed 20 of these 27 women to have pre-malignant/malignant lesions (9,7,3,1 women with CIN I,II,III and SCC respectively) (Table 5). The sensitivity, specificity, PPV, NPV of colposcopy in our study was found to be 100.00%, 30.00%, 74.07%, and 100.00% for detecting premalignant lesions of cervix. Accuracy of colposcopy was estimated to be 76.67%. Our results were similar to Gandi et al, Ashmita et al who reported a high sensitivity of colposcopy of 92.03% and 90.24%.[11,13] Ramesh et al has also reported a low specificity similar to our results.[15]

In all the accuracy of Paps and colposcopy was estimated to be 50.00%, 76.67% respectively in our study (Table 6). A higher accuracy rate with colposcopy has also been reported by Ashmita et al.[13]

We observed that combining these two procedures, the pickup rate of precancerous lesions of cervix becomes quite high, and very few cases are expected to be missed. Therefore, this combined approach is a very useful, easy, simple tool for screening pre-malignant lesions of cervix and can be done in the same sitting as an outdoor procedure.

CONCLUSION

The results of this study support that Pap smear had poor sensitivity and can miss many precancerous lesions of cervix, though its specificity is much better compared to colposcopy. Colposcopy when performed in addition to routine Pap screening in the same sitting, highly improves the pickup rate for precancerous cervical lesions. Hence, using a composite procedure of Pap smear and colposcopy, a simple outdoor procedure, greatly improves the accuracy of detecting cervical

abnormalities. We therefore, recommend utilization of both the tests for cervical pre-cancer screening.

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