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Comparison and Correlation of Cytology, Colposcopy and Histopathology of Premalignant Lesions of Cervix In Rural Women of Barabanki District

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Abstract
Aims and Objective: *(1)To record the colposcopic and cytological findings of the cases and to compare it with each other in detecting premalignant lesions of cervix taking histopathology as gold standard.(2)To correlate the findings of cytology and colposcopy with histopathology in detecting premalignant lesions of cervix.*
Materials and Methods: *This was a hospital based cross-sectional study conducted at HIMS,Barabanki.The study period was of one year.The study included pap smear samples,colposcopy reports and colposcopy guided cervical biopsy samples of 208 sexually active rural female patients of reproductive age group.*
Results: *Majority of the women were between 31-40 years(59.6%).On PAP smear,ASC-US was found in 5.8% of women,ASC-H in 1.4% of women,LSIL in 6.7% of women and HSIL in 6.2% of women.On colposcopy,LSIL was seen in 26.4% of women and HSIL in 17.8% of women.On histopathological examination,CIN I was seen in 16.8% of women followed by CIN II(8.2%)and CIN III(5.8%).Sensitivity and specificity of PAP smear was 29.7% and 94.4%.Sensitivity and specificity of colposcopy was 85.9% and 74.3%.*
Conclusion: *Pap smear had a poor sensitivity compared to colposcopy but a better specificity than colposcopy.Hence,it may be better to utilise both tests in screening of premalignant lesions of cervix as they complement each other.*
Keywords: *Premalignant Lesions of Cervix,Cytology,Colposcopy, Histopathology.*

I. Introduction

Cancer cervix is the second most common cancer in women after carcinoma breast in the world, while it is the leading cancer in women in the developing countries including India.[1] More than 80% patients present in a fairly advanced stage.[2] According to the GLOBOCAN statistics, the estimated incidence of cervical cancer in the world is 528000 per year with 266000 annual deaths attributed to cervical cancer (approximately 50%).[3] India alone contributes to 23% of the total global cases annually. With an annual 67000 deaths, cervical cancer remains one of the major causes of cancer related mortality in India.[4] Cervical intraepithelial neoplasia (CIN) is a premalignant condition of the uterine cervix.Detected in pre-malignant stages,cervical cancer is preventable and curable,so detection of premalignant lesions is very important.

II. Aims And Objective

The present study was conducted with aims and objectives to (1) to record the colposcopic and cytological findings of the cases and to compare it with each other in detecting premalignant lesions of cervix taking histopathology as gold standard; (2) to correlate the findings of cytology and colposcopy with histopathology in detecting premalignant lesions of cervix.

III. Materials And Methods

This was a hospital based cross-sectional study. The study was conducted in the Department of Pathology and Department of Obstetrics & Gynaecology, Hind Institute of Medical Sciences, Safedabad, Barabanki, U.P. The study was performed after permission from Institutional Ethics Committee. The study period was of one year(2015-2016). The study included pap smear samples, colposcopy reports and colposcopy guided cervical biopsy samples of 208 sexually active rural female patients of reproductive age group, in and

around Barabanki district (U.P) who came to the OPD of Gynaecology Department (HIMS, Barabanki,U.P.) with complaints of discharge per vagina / inter menstrual bleeding / post coital bleeding during the study period.

Samples of prepubertal and postmenopausal women who presented with gynaecological complaints, women with invasive carcinoma of cervix and other genital malignancies, pregnant and puerperial women, unmarried women and post hysterectomy cases were excluded from the study.

Methods

PAP smear samples

Pap smear samples of the female patients fulfilling the inclusion criteria were collected. Samples smeared on two glass slides (one slide with ectocervical material and a second slide with endocervical material) were received in the Pathology department in Coplin jar containing fixative- 95% ethyl alcohol or equal parts of 95% ethyl alcohol and ether. Pap smear was taken using Ayre's spatula after exposing cervix with Cusco's speculum. The prepared PAP smear slides were then stained according to the conventional PAP technique and examined under a compound light binocular microscope for cytological examination.The cytological interpretation of the smears was made according to the Bethesda System 2014 reporting criteria.[5] The findings were recorded. All these female patients were also subjected to colposcopy and colposcopy guided cervical biopsy .

Colposcopy reports

Colposcopy reports of the female patients fulfilling the inclusion criteria of this study were collected from Gynaecology Department. For colposcopy examination, PRO MIS Colposcope -model COLPRO222DX (with zoom upto 40x) was used. Colposcopy diagnosis was made based on Modified Reid's Colposcopic Index.[6,7] The findings were recorded. All these female patients underwent pap smear examination earlier and were also subjected to colposcopy guided cervical biopsy.

Colposcopy guided cervical biopsy samples

Colposcopy guided cervical biopsy samples of the female patients fulfilling the inclusion criteria of this study were collected.Biopsy specimens were received in the Pathology department in 10% formalin fixative solution.Cervical biopsy was taken from abnormal areas by punch-biopsy forceps under colposcopic guidance. The biopsied tissues were then subjected to detail gross examination.Routine tissue processing was done.Sections were cut and were stained with Haematoxylin and Eosin stain and mounted in DPX. The slides prepared were examined under a compound light binocular microscope for histopathological examination.Biopsy results were categorized according to CIN(Cervical intraepithelial neoplasia) and SIL(Squamous intraepithelial lesion) classification systems.[8] The findings were recorded.The diagnosis of premalignant lesions of cervix was based on final histopathology report obtained. All these female patients underwent PAP smear examination and colposcopy examination before they were subjected to colposcopy guided cervical biopsies.

Statistical analysis

The descriptive statistics are presented .The results are presented in percentages. The Chi-square test was used to compare the categorical variables. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for PAP smear and colposcopy taking histopathological finding as gold standard. The p-value<0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

IV. Results

Majority of the women were between 31-40 years (59.6%) followed by 41-50 years (31.2%) and <30 years (9.1%) (Table-1). On PAP smear findings, ASC-US was found in 5.8% of the women and ASC-H was found in 1.4% of the women. LSIL was found in 6.7% of the women and HSIL was found in 6.2% of the women.NILM (Negative for intraepithelial lesion or malignancy) (79.3%) was found to be in majority of the women. (Table-2).On colposcopy findings, LSIL was in 26.4% of the women and HSIL was in 17.8% of the women. Normal colposcopy was seen in 51.9% of the women. (Table-3). Histopathological finding of CIN I was seen in 16.8% of the women followed by CIN II (8.2%) and & CIN III (5.8%). Chronic cervicitis/chronic cervicitis with squamous metaplasia was seen in majority of the women (52.9%).Cervix was normal in 16.3% of women (Table-4).

With PAP smear finding of ASC-US which constitutes total 6 number of patients, correlation with histopathological findings was: 16.7 % in CIN I category, 16.7% in CIN II category and 0 in CIN III category. With PAP smear finding of LSIL which constitutes total 14 number of patients,correlation with histopathological findings was: 35.7% in CIN I category, 14.3 % in CIN II category and 7.1% in CIN III

category. With PAP smear finding of ASC-H which constitutes total 3 number of patients,correlation with histopathological findings was: 33.3% in CIN I category, 33.3 % in CIN II category and 33.3% in CIN III category.With PAP smear finding of HSIL which constitutes total 13 number of patients,correlation with histopathological findings was:15.4% in CIN I category,30.8% in CIN II category and 38.5% in CIN III category. PAP smear was significantly (p=0.0001) correlated with histopathological findings (Chi-square test). (Table-5).

With Reid's Colposcopy score 3-5(LSIL) which constitutes total 55 number of patients, correlation with histopathological findings was: 38.2% % in CIN I category, 10.9 % in CIN II category and 1.8% in CIN III category. With Reid's Colposcopy score 6-8(HSIL), which constitutes total 37 number of patients, correlation with histopathological findings was:13.5% in CIN I category,29.7% in CIN II category and 29.7% in CIN III category. Colposcopy finding was significantly (p=0.0001) correlated with histopathological finding(Chi-square test). (Table-6).

With PAP smear finding of ASC-US which constitutes total 6 number of patients, correlation with colposcopy findings was: 16.7 % in category of Reid's score 3-5(LSIL) and 16.7 % in category of Reid's score 6-8(HSIL). With PAP smear finding of LSIL which constitutes total 14 number of patients,correlation with colposcopy findings was: 21.4 % in category of Reid's score 3-5(LSIL) and 28.6 % in category of Reid's score 6-8(HSIL). With PAP smear finding of ASC-H which constitutes total 3 number of patients,correlation with colposcopy findings was: 33.3% in category of Reid's score 3-5(LSIL) and 0 in category of Reid's score 6-8(HSIL). With PAP smear finding of HSIL which constitutes total 13 number of patients,correlation with colposcopy findings was: 23.1 %in category of Reid's score 3-5(LSIL) and 15.4 % in category of Reid's score 6-8(HSIL).PAP smear was insignificantly (p>0.05) correlated with colposcopy findings (Chi-square test). (Table-7).

The sensitivity and specificity of PAP smear was 29.7% and 94.4% respectively. Accuracy of PAP smear was 74.5%.(Table-8). The sensitivity and specificity of Colposcopy was 85.9% and 74.3% respectively. Accuracy of colposcopy was 77.9% (Table-9).

Table-1: Distribution of women according to age

Age in years	No. (n=208)	%
<30	19	9.1
31-40	124	59.6
41-50	65	31.2

Table-2: Distribution of women according to PAP smear findings

PAP smear findings	No. (n=208)	%
NILM	165	79.3
ASC-US	6	5.8
LSIL	14	6.7
ASC-H	3	1.4
HSIL	13	6.2
Unsatisfactory smear	7	3.4

Table-3: Distribution of women according to Colposcopy findings

Colposcopy findings(REID'S SCORE)	No. (n=208)	%
Score 0-2 (Normal colposcopy)	108	51.9
Score 3-5(LSIL)	55	26.4
Score 6-8(HSIL)	37	17.8
Unsatisfactory Colposcopy	8	3.8

Table-4: Distribution of women according to Histopathology findings

Histopathology findings	No. (n=208)	%
Normal	34	16.3
Chronic cervicitis /chronic cervicitis with metaplasia	110	52.9
CIN I	35	16.8
CIN II	17	8.2
CIN III	12	5.8

Table-5: **Correlation of PAP smear with histopathological findings**

PAP Smear	Total	Histopathological findings									
		Normal		Chronic cervicitis/ chronic cervicitis with metaplasia		CIN I		CIN II		CIN III	
		No.	%	No.	%	No.	%	No.	%	No.	%
NILM	165	31	18.8	97	58.8	25	15.1	8	25.8	4	2.4
ASC-US	6	1	16.7	3	50	1	16.7	1	16.7	0	0
LSIL	14	0	0	6	42.8	5	35.7	2	14.3	1	7.1
ASC-H	3	0	0	0	0.0	1	33.3	1	33.3	1	33.3
HSIL	13	0	0	2	15.4	2	15.4	4	30.8	5	38.5
Unsatisfactory smear	7	2	57.1	2	28.6	1	14.3	1	14.3	1	14.3
Total	208	34	16.3	110	52.9	35	16.8	17	8.2	12	5.8

p=0.0001 (Chi-square test)

Table-6: Correlation of Reid's Colposcopy score with histopathological findings

Reid's score	Total	Histopathological findings									
		Normal		Chronic cervicitis/ Chronic cervicitis with metaplasia		CIN I		CIN II		CIN III	
		No.	%	No.	%	No.	%	No.	%	No.	%
Normal (REID'S SCORE-0-2)	108	24	22.2	75	69.4	9	8.3	0	0	0	0
LSIL (REID'S SORE-3-5)	55	5	9.1	22	40	21	38.2	6	10.9	1	1.8
HSIL (REID'S SCORE-6-8)	37	2	5.4	8	21.7	5	13.5	11	29.7	11	29.7
Unsatisfactory colposcopy	08	3	37.5	5	62.5	0	0	0	0	0	0
Total	208	34	16.3	110	52.9	35	16.8	17	8.2	12	5.8

p=0.0001 (Chi-square test)

Table-7: Correlation of PAP smear with colposcopy findings

PAP smear	Total	Colposcopy findings							
		Normal (REID'S SCORE-0-2)		LSIL (REID'S SORE-3-5)		HSIL (REID'S SCORE-6-8)		Unsatisfactory colposcopy	
		No.	%	No.	%	No.	%	No	%
NILM	165	86	52.1	46	27.9	29	17.6	4	2.4
ASC-US	6	4	66.7	1	16.7	1	16.7	0	0
LSIL	14	7	50	3	21.4	4	28.6	0	0
ASC-H	3	2	66.7	1	33.3	0	0	0	0
HSIL	13	6	46.15	3	23.1	2	15.4	2	15.4
Unsatisfactory smear	7	3	42. 8	1	14.3	1	14.3	2	28.6
Total	208	108	51.9	55	26.4	37	17.8	8	3.8

p=0.11 (Chi-square test)

Table-8: Diagnostic efficacy of PAP smear test

	Histopathology		
PAP smear	Positive	Negative	Total
Positive	19	8	27
Negative	45	136	181
Total	64	144	208
Sensitivity	29.7 %		
Specificity	94.4%		
PPV	70.4%		
NPV	75.1%		
Accuracy	74.5%		

Table-9: Diagnostic efficacy of Colposcopy test

	Histopathology		
Colposcopy	Positive	Negative	Total
Positive	55	37	92
Negative	9	107	116
Total	64	144	208
Sensitivity	85.9%		
Specificity	74.3%		
PPV	59.8%		
NPV	92.2%		
Accuracy	77.9%		

V. Discussion

Cervical intraepithelial neoplasia (CIN) is a premalignant lesion that may exist at any one of three stages: CIN1, CIN2, or CIN3.If left untreated, CIN2 or CIN3 (collectively referred to as CIN2+) can progress to cervical cancer. It is estimated that approximately 1–2% of women have CIN2+ each year.[9,10,11]

The present study included pap smear samples, colposcopy reports and colposcopy guided cervical biopsy samples of 208 sexually active rural female patients of reproductive age group. In the present study, majority of the women were between 31-40 (59.6%) years followed by 41-50 (31.2%) and <30 (9.1%) years.

In the present study, on PAP smear, ASC-US was found in 5.8% of the women and ASC-H was found in 1.4% of the women .LSIL was found in 6.7% of the women and HSIL was found in 6.2% of the women. NILM (79.3%) was found to be in majority of the women. Similar findings were seen in previous studies done by Ashmita et al (2013)[12], Chaudhary et al (2014)[13], Joshi et al (2015)[14] and various others.

In the present study, on colposcopy findings, LSIL was in 26.4% of the women and HSIL was in 17.8% of the women. Unsatisfactory colposcopy was in 3.8 % of the women. Normal colposcopy was seen in 51.9% of the women. Similar findings were seen in previous studies done by Ashmita et al (2013)[12], Chaudhary et al (2014)[13],Joshi et al (2015)[14], Krishnegowda and Veena (2014)[15] and various others.

In the present study, histopathological finding of chronic cervicitis/chronic cervicitis with squamous metaplasia was seen in majority of the women (52.9%). CIN I was seen in 16.8% of the women followed by CIN II (8.2%) and & CIN III (5.8%). Normal cervix was seen in 16.3% of women. Similar findings were seen in previous studies done by Joshi et al (2015)[14], Gopal et al (2013)[16], Chaudhary et al (2014)[13], Bodal and Brar (2014)[17] and various others.

In the present study, PAP smear findings were significantly (p=0.0001) correlated with histopathological findings .This finding is similar to the results of the study done by Nayani and Hendre (2015)[18], Bukhari et al (2012)[19], Ashmita et al (2013)[12] and various others.

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In the present study, PAP smear findings were insignificantly (p>0.05) correlated with coposcopy findings.This finding is similar to the results of the study done by Nayani and Hendre (2015)[18], Bukhari et al (2012)[19], Ashmita et al (2013)[12] and various others.

In the present study, the sensitivity of PAP smear was 29.7% , specificity was 94.4%, PPV was 70.4%, NPV was 75.1% and accuracy was 74.5% for diagnosing premalignant lesions of cervix. The accuracy of pap smear in our study was 74.5% which is comparable to the findings of the studies of Chaudhary et al (2014)[13] (76%), Bhatla et al (2007)[20] (89%), Maziah et al (1991)[21] (90%), Jain et al (2010)[22] (73.2%), Saha et al (2005)[23] (79.1%), Naik et al (2015)[24] (74.5%). However, Mallur et al (2009)[25] and Ashmita et al (2013)[12] concluded the accuracy of PAP smear to be 40% and 33.96%

In the present study, the sensitivity of Colposcopy was 85.9%,specificity was 74.3%, PPV was 59.8%, NPV was 92.2% and accuracy was 77.9% for diagnosing premalignant lesions of cervix. The accuracy of colposcopy in this study was 77.9% which is in parallel to the findings of the studies of Maziah et al(1991)[21] (94%), Ashmita et al (2013)[12] (86.54%), Mallur et al (2009)[25] (80%), Chaudhary et al (2014)[13] (80.50%) and Boicea et al (2012)[26] (98.3%).

Literature is replete with data pertaining to the sensitivity of Pap smear and colposcopy ranging from 27% to 50% vs 44%-89% respectively. Specificity of Pap smear and colposcopy ranging from 19.5%-98.71% vs 52%-93.4% respectively.[12,13,25,27,28] In the present study,overall Pap smear had a poor sensitivity compared to colposcopy, 29.7% vs 85.9 % respectively. Pap smear had a better specificity though not significantly compared to colposcopy, 94.4% vs 74.3 % respectively.

The incidence of premalignant lesions of cervix in our study was 30.8 %. The incidence of premalignant lesions of cervix in various studies range from 8.15% to 35.2%.[12,13,25,27,29,30]

The main goal of cervical screening is to identify women with premalignant lesions of cervix which are precursors of invasive cancer and require treatment, thus ultimately decreasing morbidity and mortality due

to cervical cancer. The results from the current study support the claim to perform combination screening tests as part of routine screening for cervical cancer screening rather than pap smear alone in order to detect maximum number of cases with accuracy and minimal loss of patients to follow up.

VI. Conclusion

Pap smear had a poor sensitivity compared to colposcopy. Pap smear had a better specificity though not significantly compared to colposcopy. Hence, it may be better to utilise both tests in screening of premalignant lesions of cervix as they complement each other.

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