

Role of Colposcopy in the Evaluation of Unhealthy Cervix and Cervical Intraepithelial Neoplasia

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ABSTRACT

BACKGROUND

Invasive cancer of cervix is preventable because it has a long pre-invasive phase, cervical cytology screening is possible, and the treatment of pre-invasive lesions is effective. There are various methods available for screening of cervical precancerous and cancerous lesions like Visual Inspection by Acetic Acid (VIA), Visual inspection by Lugol's Iodine (VILI), conventional pap smear, liquid based cytology, colposcopy and HPV DNA testing. But, negative cytology does not rule out cervical intraepithelial lesions (CIN) completely. In this study we have studied patients with symptoms, abnormal appearing cervix, and patients with abnormal cytology by colposcopy to detect intraepithelial neoplasia of cervix.

METHODS

In this cross-sectional observational study of 149 subjects, women attending outpatient department of Obstetrics and Gynaecology who were symptomatic for recurrent and persistent vaginal discharge, postcoital bleeding, menstrual abnormalities were examined by per speculum examination and cervical cytology obtained. In indicated patients, colposcopy was done and colposcopic directed biopsy of lesions was taken for evaluation and the results compared.

RESULTS

Colposcopy showed accurate estimation in 57.89% cases, over estimation in 36.84% cases and under estimation in 5.26% cases. Sensitivity of colposcopy in our study was 98.30%. Specificity of colposcopy in present study was 57.30%. Positive predictive value of colposcopy in our study was found to be 68.75%, negative colposcopy value was 96.66%. Prevalence of CIN in our study group was found to be 39.43%.

CONCLUSIONS

Colposcopy was found to be useful in understanding the morphology of the cervical lesions, both of the benign and neoplastic and this was very helpful in planning their management. In spite of less specificity and less positive predictive value in our study, a detailed colposcopic evaluation of cervix with a guided biopsy is recommended as an important diagnostic method for the detection of precancerous lesions and early cervical cancer.

KEYWORDS

Unhealthy Cervix, Colposcopy, Cervical Intraepithelial Neoplasia (CIN), Cytology, Punch Biopsy

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DOI: 10.18410/jebmh/2020/317

*Financial or Other Competing Interests:
None.*

How to Cite This Article:

Fuke RP, Sonak M, Singh M. Role of colposcopy in the evaluation of unhealthy cervix and cervical intraepithelial neoplasia. J. Evid. Based Med. Healthc. 2020; 7(30), 1506-1511. DOI: 10.18410/jebmh/2020/317

*Submission 24-04-2020,
Peer Review 05-01-2020,
Acceptance 28-05-2020,
Published 27-07-2020.*

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BACKGROUND

Cervical cancer is the second most common cancer in women in India.¹ Invasive cancer of cervix has been considered a preventable cancer because it has a long pre-invasive state, cervical cytology screening programs are available and the treatment of pre-invasive lesions is effective.² The unique accessibility of the cervix to direct visualization and the possibility of cellular and tissue sampling has permitted extensive investigations on lesions of cervix. There are various methods available for screening of cervical precancerous and cancerous lesions like visual inspection by acetic acid (VIA), Visual inspection by Lugol's Iodine (VILI), conventional pap smear, liquid based cytology, colposcopy and HPV (Human Papilloma Virus) DNA testing.^{3,4}

But, the naked eye evaluation of unhealthy cervix is deceptive sometimes and so is the cytology as negative cytology does not rule out cervical intraepithelial lesions (CIN) completely. Unhealthy cervix and abnormal pap smears need further evaluation and confirmation by colposcopy and colposcopic directed punch biopsy of cervical lesions.⁵ Screening of the cervix by cytology and colposcopy can significantly reduce the cases of invasive cancers.^{6,7}

Aim

To assess the role of colposcopy in the detection of pre-invasive lesions of cervix.

Objectives

1. To estimate the prevalence of cervical intraepithelial neoplasia in study group.
2. To detect the abnormal cervical lesions by cytology and colposcopy.
3. To correlate colposcopic findings with histopathology examination of colposcopic directed punch biopsy.
4. To determine the sensitivity and specificity of colposcopy as a screening tool for diagnosis of Cervical Intraepithelial neoplasia.

METHODS

This is a cross sectional observational study conducted between January 2019 to December 2019, among a total of 149 study subjects. We have included all the patients who underwent colposcopy and colposcopic directed biopsy in the duration study period. The study was carried out in the OPD of Department of Obstetrics and Gynaecology at a Tertiary care hospital.

Inclusion Criteria

1. Women who gave consent for the study.
2. Women of age between 20-65 years with symptoms like vaginal discharge, postcoital bleeding, postmenopausal

bleeding, inter menstrual bleeding and persistent leucorrhoea not responding to antibiotics.

3. Women with suspicious cervical lesions.
4. Women with abnormal pap smear findings.

Exclusion Criteria

1. Women with bleeding at the time of examination.
2. Women with frank malignant lesions of lower genital tract.
3. Women who had been previously treated for carcinoma cervix.
4. Pregnant women.

All women attending outpatient department of Obstetrics and Gynaecology who were symptomatic for vaginal discharge, postcoital bleeding, menstrual abnormalities, pain in abdomen and persistent and recurrent leucorrhoea were examined by per speculum examination. Pap smear was done in each patient as per recommendation. Those patients who fulfilled one or more inclusion criteria were subjected to colposcopic examination and colposcopic directed biopsy of lesions with the help of punch biopsy forceps after taking informed written consent. The punch biopsy was sent for histopathological examination and observations tabulated as follows.

RESULTS

Age (Years)	No. of Subjects (n)	%
21-25	10	6.71
26-30	28	18.79
31-35	30	20.13
36-40	24	16.10
41-45	25	16.77
46-50	21	14.09
51-55	07	4.69
>55	04	2.68
Total	149	100

Table 1. Distribution of Cases According to Age

Reproductive Characteristics	No. of Subjects (n)	%
Reproductive	118	79.19
Perimenopausal	17	11.40
Menopausal	14	9.39
Sexually active	125	83.89
Sexually not active	24	16.10
Nulliparous	11	7.38
Para 1	34	22.81
Para 2	52	34.89
Para 3	29	19.46
Para 4 and >	09	6.04

Table 2. Distribution of Cases According to Reproductive Age, Sexual Activity, and Parity

Indication for Colposcopy/ Presenting Complaints	No. of Subjects (n)	%
Vaginal discharge	63	42.28
Abdominal pain	12	8.05
Abnormal cervix	18	12.08
Abnormal pap smear	22	14.76
Cervical erosion	09	6.04
Post coital bleeding	08	5.36
Follow up of previous intraepithelial lesions	03	2.01
Miscellaneous	14	9.39
Total	149	100

Table 3. Distribution of Cases According to Indication for Colposcopy

Cytology Report	No. of Subjects (n)	%
Not taken	12	8.05
Normal	16	10.73
Inflammatory	75	50.33
LSIL	16	10.73
HSIL	4	2.68
ASCUS	19	12.75
Metaplasia	3	2.01
Not satisfactory	3	2.01
Others	1	0.67
Total	149	100

Table 4. Distribution of Cases According to Cytology Findings

Colposcopy	No. of Subjects (n)	%
Satisfactory	135	90.60
Not satisfactory	14	9.39
Total	149	100

Table 5a. Distribution of Cases According to Colposcopy Findings

Squamo Columnar Junction	No. of Subjects (n)	%
Completely visible	105	70.46
Partially visible	28	18.79
Invisible	16	10.73
Total	149	100

Table 5b

Transformation Zone	No. of Subjects (n)	%
TZ 1	103	72.53
TZ 2	22	15.49
TZ 3	17	11.97
Total	142	100

Table 5c

Swede Score	No. of Subjects (n)	%
0-4	81	57.04
5-6	40	28.16
7-10	21	14.78
Total	142	100

Table 5d

Diagnosis on Colposcopy	No. of Subjects (n)	%
Normal	15	10.56
Cervicitis	6	4.22
Cervical ectropion	19	13.38
LSIL	51	35.91
HSIL	28	19.71
Invasive carcinoma	1	0.70
Immature squamous metaplasia	19	13.38
Miscellaneous	3	2.11
Total	142	100

Table 5e

Biopsy Report	No. of Patients	%
Normal	19	13.38
Inflammation	23	16.19
Metaplasia	39	27.46
LSIL	40	28.16
HSIL	14	9.85
Squamous cell carcinoma	03	2.11
Miscellaneous	04	2.11
Total	142	100

Table 6. Distribution of Cases According to Histopathology Findings of Punch Biopsy

Colposcopic Diagnosis	Histopathology Findings					
	Normal	Inflammation	Metaplasia	LSIL	HSIL	Invasive Carcinoma
Normal	13	1	1	-	-	-
Inflammation	-	6	-	-	-	-
Metaplasia	-	2	6	1	-	-
LSIL	4	-	18	28	1	-
HSIL	-	-	3	10	13	2
Invasive carcinoma	-	-	-	-	-	1

Table 7. Correlation of Colposcopy with Histopathological Findings

Colposcopy Results	Under Estimation	Accurate Estimation	Over Estimation
Normal	2	13	0
LSIL	1	28	22
HSIL	2	13	13
Invasive carcinoma	0	1	0
Total	5 (5.26%)	55 (57.89%)	35 (36.84%)

Table 8. Evaluating Validity of Colposcopy with Histopathology

Colposcopy	Biopsy		Total
	Positive	Negative	
Positive	TP 55	FP 25	80
Negative	FN 1	TN 29	30
Total	56	54	110

Table 9

$$\text{Sensitivity} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Negative}} \times 100$$

$$\frac{55}{56} \times 100 = 98.21\%$$

$$\text{Specificity} = \frac{\text{True negative}}{\text{True negative} + \text{False positive}} \times 100$$

$$\frac{29}{54} \times 100 = 53.70\%$$

Positive Predictive Value

$$= \frac{\text{True Positive}}{\text{True Positive} + \text{False Positive}} \times 100$$

$$\frac{55}{80} \times 100 = 68.75\%$$

Negative Predictive Value

$$= \frac{\text{True Negative}}{\text{False Negative} + \text{True Negative}} \times 100$$

$$\frac{29}{30} \times 100 = 96.66\%$$

$$\text{Prevalence} = \frac{56}{142} \times 100 = 39.43\%$$

Amongst 149 cases, maximum subjects were in the age group of 31-35 years (20.13%) followed by 28 subjects in 26-30 years (18.79%), 25 cases in 41- 45 years (16.77%) followed by 24 cases in 36-40 years category (16.10%). There were 21 cases in 46-50 years age group (14.09%) and relatively less (10 cases) among 21- 25 years (6.71%) and least after 55 years (2.68%).

There were 118 subjects (79.19%) in reproductive age group, 17 (11.40%) were perimenopausal and 14 women (9.39%) were in established menopause. There were 125 women (83.89%) in the study who were sexually active that put them to the risk of acquiring sexually transmitted diseases and HPV infection. Maximum women (52) were para 2 (34.89%) followed by para 1 (22.81%) and para 3 (19.46%). The main presenting complaint was vaginal discharge in 63 women (42.25%) followed by abdominal pain.

The main indications for colposcopy were also vaginal discharge in 42.25% and abnormal looking cervix in 18 women (12.08%) and abnormal pap smear in 14.765 women. The other indications were cervical erosion (6.04%), post coital bleeding (5.36%), follow-up of previous intraepithelial lesions (2.01%) and other lesions (condyloma, polyp, etc.) in 9.39% subjects. Cervical cytology by Pap smears were done in almost all women except 12 (8.05%) women due to some or the other reason.

The most common finding in cervical cytology was inflammatory smear in 75 (50.33%) women followed by Atypical squamous cells of undetermined significance (ASCUS) in 19 (12.75%) cases, 16 cases (10.73%) were reported as LSIL (Low Grade Squamous Intraepithelial Lesions) and 4 (2.68%) as HSIL (High Grade Squamous Intraepithelial Lesions). Sixteen (10.73%) Pap smears were normal.

Out of 149 cases who were subjected to colposcopy, the examination was satisfactory in 135 cases (90.60%) and not satisfactory in 14 cases (9.39%) because of improper visualisation of cervix due to position or lax collapsing vaginal walls or obscured by bleeding. Squamo-columnar junction was completely visualised in 105 (70.46%) patients on colposcopy and partially visible in 28 (18.79%) of cases. The squamo-columnar junction was invisible in 16 (10.73%) of cases. This corresponds to the fact that 9.39% of women in study were menopausal in whom squamo-columnar junction is usually receded in endocervical canal and not visible on colposcopy. Type 1 transformation zone (TZ) was found in 103 (72.53%) cases while type 2 TZ and type 3 TZ was found in 22 (15.49%) and 17 (11.97%) cases, respectively. If we divide the cases according to Swede score, 0-4 score was found in 81 i.e. 57.04% of cases while 5-6 score was observed in 40 (28.16%) cases and 7-10 Score was seen in 21 (14.78%) of cases.

Overall 35.91% of cases were diagnosed as LSIL and 19.71% of cases were diagnosed as HSIL on colposcopy with 13.38% of cases of cervical ectropion and immature squamous metaplasia. Invasive carcinoma was diagnosed in 1 (0.70%) patients and cervicitis in 4.22% of cases and miscellaneous findings were observed in 3 cases (2.11%). Colposcopy was normal in 15 (10.56%) of cases.

All the cases were subjected to colposcopic directed punch biopsy as it is the gold standard for the diagnosis of intraepithelial lesions. On histopathological examination, LSIL was diagnosed in 40 (28.16%) cases followed by metaplasia in 39 (27.46%) of cases. Inflammation was diagnosed in 23 (16.19%) of cases and HSIL was diagnosed in 14 cases (9.85%). Squamous cell carcinoma was diagnosed in 3 cases (2.11%) and miscellaneous lesions in 4 cases (2.11%). Biopsy revealed no abnormality in 19 cases (13.38%)

Out of 51 women who were likely to be LSIL on colposcopy, 28 were having LSIL, 18 had metaplasia and 1 had HSIL and 4 women showed normal results on histopathology. Out of 28 women who were likely to be HSIL on colposcopy, 13 women were having HSIL, 10 had LSIL, 3 women had metaplasia and 2 women had invasive

carcinoma on biopsy. Out of 1 woman who suspected to have invasive carcinoma on colposcopy had invasive squamous cell carcinoma on biopsy. Out of 15 normal reports on colposcopy, 13 were normal, 1 had inflammation and 1 woman had metaplasia on biopsy. Out of 6 cases who were having inflammatory findings on colposcopy, all had inflammatory picture in biopsy. Out of 9 cases who had metaplasia on colposcope, 6 women were having metaplasia, 2 had inflammation and 1 woman had LSIL. Out of 95 cases, Total 35 cases (36.84%) were overestimated, 55 (57.89%) cases were accurately estimated and 5 (5.26%) cases were underestimated on colposcopy when compared with histopathology reports.

Present study shows that colposcopy has a good sensitivity and specificity of 98.21% and 53.70% respectively. Positive predictive value and negative predictive value of the test were 68.75% and 96.66% respectively. The Prevalence of intraepithelial neoplasia in the study group calculated out to be 39.43%.

In our study, it was observed that-

1. Most of the subjects were in the age group of 31-40 years, in the reproductive age group and sexually active. Most of the cases were para 2 and para 1
2. White discharge per vagina (45.83%) has been observed to be the most common complaint and also the indication for colposcopy followed by abnormal looking cervix and abnormal pap smear.
3. 61.06% patients showed normal (Inflammation included) Pap smear reports.
4. According to swede score in our study, 0-4 score was found in 81 i.e. 57.04% of cases while 5-6 score was observed in 40 (28.16%) cases and 7-10 Score was seen in 21(14.78%) of cases and not satisfactory in 14 cases (9.39%)
5. 38.01% cases had intraepithelial lesion of cervix on histopathological reports.
6. Colposcopy showed accurate estimation in 57.89% cases, over estimation in 36.84% cases and under estimation in 5.26% cases. The number of overestimated cases was more as compared to others and that was the drawback of the study.

Sensitivity of colposcopy in our study was 98.30%. Specificity of colposcopy in present study was 57.30%. Positive predictive value of colposcopy in our study was found to be 68.75%, negative colposcopy value was 96.66%. Prevalence of CIN in our study group was found to be 39.43%.

DISCUSSION

Though cervical cytology is the effective screening tool for cervical cancer, negative cytology does not rule out CIN and invasive cancers. Colposcopy has added advantage of localising and determining the extent of lesion, selecting the site of biopsy in the same setting, managing the treatment part and follow up of patients.⁸ This study focused on the fact that colposcopy forms an important tool in the diagnosis and management of CIN. The results were compared with

the studies done already and to most of the extent, the results were comparable.

In the study conducted by Kalyankar VY et al,⁹ Patil P et al,¹⁰ Dharaiya N et al,¹¹ the maximum patients were in the age group of 31- 40 years (39%,39.2%,38.5% and 47.4% respectively), a finding similar to many studies like Pandey et al,¹² Goel et al¹³ and Durdi G et al.¹⁴ in our study also, maximum cases belong to 31-35 and 26-30 years of age group (38.9%), reproductive age group (79.19%) and 83.89% were sexually active. This is the age group who are at the risk of acquiring the sexually transmitted HPV infections and CINs. The pathogenesis of precancerous lesions starts in this decade. Thus, the importance of screening for cervical neoplasia in this age group cannot be overemphasised.

In the study by Goel et al, Durdi G et al and Kalyankar VY et al, majority cases were para 2 (30.8%) and para 3 (27.9%). We had maximum cases who were para 2 followed by para1 and para 3. Incidence of CIN increases as the parity increases.

Durdi G et al in their study reported that 66% patients had vaginal discharge as the most common complaint and 5.1% of cases with postcoital bleeding. Similarly, Bharati B et al¹⁵ and Patil P et al had 52% and 6.28%, 52.8% and 6% of cases of vaginal discharge and postcoital bleeding, respectively. Most of our study population presented with the same complaint of vaginal discharge (42.25%) which was also the main indication for colposcopy followed abnormal Pap smear reports in 14. 76% of cases and abnormal cervix in 12.08% cases.

The most common finding in cervical cytology was inflammatory smear (50.33%) followed by ASCUS (12.75%), LSIL (10.73%) and HSIL (2.68%). Normal Pap smear reports were seen in 10.73% of cases. In a study by Denny L et al, 84.8% of Pap smear were normal (inflammation included), 7% ASCUS, 3% LSIL, @ 0.7% HSIL and 0.1% had invasive carcinoma.¹⁶

In our study we observed that Satisfactory and unsatisfactory colposcopic examinations were 90.60% and 9.39% whereas in studies conducted by Bharti B et al, Patil P et al and Kalyankar V. Y et al the unsatisfactory colposcopic examination was seen in 7.4%, 2.5% and 2% and by Ramesh G et al¹⁷ and Parvin S et al,¹⁸ the unsatisfactory examination was seen in 11.25% and 3.84%, respectively. Our studies are comparable to all these studies.

Kalyankar VY et al observed in their study that colposcopy showed 25 to be CIN 1,19 to be CIN 2 and 3 to be CIN 3 whereas on histopathology 15 women were CIN1, 21 were CIN 2and 5 were CIN3. Carcinoma cervix was found in 1 woman. Correlation in their study was found to be 78.3%. Bangal V B et al¹⁹ conducted a similar study on colposcopy where it was observed that colposcopy showed 5 cases of CIN1, 18 cases of CIN2 and 7 cases of CIN3 whereas on histopathology 11 women were CIN1, 3 were CIN2, 4 were CIN3 and 2 showed carcinoma. Thus, the correlation between colposcopy findings and histopathology was 95%. In our study, overall 51 cases were diagnosed as LSIL and 28 cases were diagnosed as HSIL on colposcopy

and invasive carcinoma was diagnosed in 1 patient. On histopathological examination, LSIL was diagnosed in 40 cases, HSIL was diagnosed in 14 cases. Squamous cell carcinoma was diagnosed in 3 cases. Thus, the histopathological correlation with colposcopy was 78.57% in our study which was similar to others.

In studies conducted by Durdi G et al, Patil P et al and Kalyankar V Y et al accurate estimation of CIN was seen in 74%,78.3% and 72% cases respectively whereas overestimation of CIN was seen in 22%,24% and 6.5% cases respectively and underestimation of CIN was seen in 4%, 4% and 15.2% cases respectively, whereas in our study we observed that 57.89%, 36.84% and 5.26% cases accurately, over and under estimated on colposcopy when compared with histopathology findings .This proves that combining colposcopy with histopathology is helpful in diagnosing CIN accurately .

In studies conducted by Ghosh P et al²⁰ sensitivity and specificity of colposcopy was 84. 2% and 97.6% respectively, while in study of Durdi G et al these were 88.5% and 86.2% respectively. Study conducted by Kalyankar V Y et al sensitivity was 90.47%, specificity was 76.92%, positive predictive value was 92.68% and negative predictive value was 71.42%. In our study the sensitivity was 98.30%, specificity was 57.30%, positive predictive value was 68.75% and negative predictive value was 96.66%. The Prevalence of the study group came out to be 39.43%. The less specificity of colposcopy in our study was because majority of subjects who were diagnosed as LSIL, histopathologically were proven to be of metaplasia so the positive predictive value was also less as compared to other studies.

CONCLUSIONS

Though Pap smear has been used as a screening method conventionally in India, studies have shown that it has low sensitivity. Moreover, there is a need of trained personnel, laboratory infrastructure, and need for compliance with follow up. Colposcopy was found to be useful in understanding the morphology of the cervical lesions, both of the benign and neoplastic, and this was very helpful in planning their management. In spite of less specificity and less positive predictive value in our study, a detailed colposcopic evaluation of cervix with a guided biopsy is an important diagnostic method for the detection of precancerous lesions and early cervical cancer. Small sample size limited the scope of further evaluation.

Financial or Other Competing Interests: None.

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