

# EVALUATE THE ROLE OF ENDOCERVICOSCOPY AND CORRELATE THE ENDOCERVICAL FINDINGS WITH FINAL HISTOPATHOLOGICAL DIAGNOSIS

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*Received Date: 28/11/2023*

*Acceptance Date: 13/12/2023*

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## Abstract

**Background:** Cervical cancer is a major cause of deaths due to cancers among women worldwide. Screening of cancer cervix at an early stage not only decrease the mortality but also the morbidity among women of developing countries. Various methods have been tried to visualize the entire TZ which include the use of endocervical speculum, osmotic dilators including laminaria and lamicel, use of ethinyl estradiol, and misoprostol. However, these techniques have a limited success rate and in around 30-40% cases TZ cannot be visualised completely. **Methodology-** The study was carried out in the Department of Obstetrics and Gynaecology and Department of Pathology at a tertiary care hospital from December 2013 to April 2015. 40 patients fulfilling the inclusion and exclusion criteria were included in the study. After taking an informed written consent from all the subjects, a complete medical and gynaecological examination was performed and baseline data was recorded and endocervicoscopy was performed. Data was analyzed and entered into Microsoft excel sheet. **Result-** On colposcopic examination, all patients had adequate colposcopy with T3 TZ i.e. upper margin of TZ was inside the endocervical canal. Of the 40 patients, SCJ was partially visible in 22 patients (55%) and completely invisible in 18 patients (45%). Colposcopy findings of the visible TZ on ectocervix were normal in 2 patients (5%). Remaining 38 patients (95%) had abnormal findings out of which 30 patients had grade 1 lesion, 7 patients had grade 2 lesions and 1 patient had non-specific changes. The above study visualize the complete SCJ in all the cases. **Conclusion-** Endocervicoscopy was found to be 100%

successful in visualization of the SCJ in all the cases. The positive predictive value (PPV) of endocervicoscopy in our study was 33.3% and negative predictive value (NPV) was 100%. The use of endocervicoscopy in cases of T3 TZ on colposcopy is recommended.

**Keywords-** Endocervicoscopy, cervix, cancer, histopathology, colposcopy.

## Introduction

Cancer of cervix is a major cause of deaths due to cancers among women worldwide. More than 5,30,000 new cases of cancer cervix are reported annually. Around 85% of these cases and deaths occur in women of developing countries<sup>1</sup>. There is a long time period from acquiring the disease to the development of pre-malignant lesions and then to frank malignancy. This long natural history of the disease provides us the opportunity to diagnose it at an early stage.

Screening of cancer cervix at an early stage not only decrease the mortality but also the morbidity among women of developing countries. Various screening modalities includes Pap smear testing, visual inspection after the application of acetic acid (VIA) and lugol's iodine (VILI), colposcopy, HPV DNA testing, cervicography<sup>2</sup>.

Colposcopy is a gold standard screening modality which compliments cytology in detecting pre-malignant and malignant lesions of cervix<sup>3</sup>. It provides a magnifying view of the transformation zone of the cervix. Transformation zone (TZ) is defined as the area of the cervix between the new and the original squamo-columnar junction (SCJ)<sup>4</sup>. TZ has high rate of active immature cell proliferation<sup>4,5</sup>. Around 90% of cervical cancer originates here<sup>6</sup>. Thus, evaluation of transformation zone is important in identifying the lesion, estimating the extent and severity of the lesion. According to the new terminology for colposcopic findings given by the IFCPC (International Federation for Cervical Pathology and Colposcopy) in 2011, TZ is divided into 3 types, i.e. T1, T2 and T3 TZ<sup>7</sup>. 10-25% of the women have T2 and T3 TZ<sup>4,5</sup>. In these women it is difficult to visualize the complete squamo-columnar junction, which lies within the endocervix. This may lead to difficulty in diagnosing any abnormal area on TZ and in evaluating the upper limit of a lesion if present. Thereby, inability to detect a lesion in T3 TZ is a major limitation of colposcopy. In a study done by Bifulco et al. in 2010, endocervicoscopy using a hysteroscope has been proposed as a novel and promising technique for evaluation of an incompletely visualised TZ<sup>7</sup>. In this method, conventional hysteroscope is used for evaluating the entire TZ after application of 5% acetic acid. Its advantage lies in the fact that it allows visualization of the entire transformation zone even if the new SCJ has receded inside the endocervix. Thus, complete extension and topography of the lesion can be assessed, thereby reducing the size of cone biopsy. Despite thorough literature search, no study has been found which has evaluated this technique in Indian population and world literature is scanty.

Therefore, the above study was conducted to evaluate the role of endocervicoscopy and correlate the endocervical findings with final histopathological diagnosis.

## Materials And Methods

**Study place-** The above study was carried out in the Department of Obstetrics and Gynaecology and Department of Pathology, UCMS & GTB Hospital, Delhi from December 2013 to April 2015.

**Study design-** Descriptive analytical study.

**Inclusion criteria-** Patients with T3 TZ (squamo-columnar junction was incompletely or completely invisible) who were referred to the colposcopy clinic due to Abnormal Pap smear, Positive VIA (visual inspection with acetic acid) or VILI (visual inspection with lugol's Iodine) and ready to give written consent.

**Exclusion criteria-** Patients having vulvo-vaginitis and acute cervicitis, active bleeding per vaginum, pregnant women and those who refused to give informed written consent.

**Sample size-** 40 women.

**Data Analysis-**Data was analyzed using SPSS version 20.0 and entered into Microsoft excel sheet. Positive predictive value (PPV) and Negative predictive value (NPV) of the technique were calculated by the standard formula. Numerical variables have been expressed as mean±SD.

**Ethical consideration-** Prior ethical clearance was taken from the Institutional Ethical Committee.

After taking an informed written consent from all the subjects, a complete medical and gynaecological examination was performed and baseline data was recorded according to the enclosed proforma. Endocervicopy was done under local, regional or general anaesthesia depending on the patient profile. The anterior and posterior lateral walls of the endocervix was carefully examined. It was noted whether the entire SCJ was identified or not. Once the SCJ was identified, it was localised in its entire path. Nabothian cysts, endocervical polyps, growth, acetowhite lesions and suspect invasive cancer were identified. The vascularisation and morphology of the endocervical mucosa was evaluated. An endocervical curettage (ECC) was taken in all the cases and cervical biopsy from the target area was taken wherever indicated at the same setting. According to the diagnosis, patients were offered excisional treatment i.e. LEEP, cone biopsy, hysterectomy.

## Result

**Table 1: Age distribution of the patients**

Age (years)	Number N=40	
	n	(%)
21-30	02	(05.0)
31-40	13	(32.5)
41-50	10	(25.0)
51-60	11	(27.5)
>60	04	(10.0)
Mean age (years) (mean±SD)	47.23±11.32	

Age of the patients varied from 26 to 70 years with mean age of 47.23±11.32 years. Majority of patients were in the age group of 31-40 years.

**Table 2: Details of colposcopic findings with T3 TZ**

Colposcopic Findings	Number N=40	
	n	(%)
General assessment		
Adequate	40	(100.0)
Inadequate	0	(0)
SCJ visibility		
Partially visible	22	(55.0)
Not visible	18	(45.0)
Colposcopic findings of visible TZ on ectocervix		
Normal	02	(05.0)
Abnormal		
<i>Grade I</i>	30	(75.0)
<i>Grade II</i>	07	(17.5)
<i>Non-specific (I<sub>2</sub> negative)</i>	01	(02.5)
Suspicious for invasion	0	(0)
Miscellaneous findings		
Polyps protruding through cervical os	03	(07.5)
Lichen planus patch	01	(02.5)

Colposcopy was adequate in all the patients. All the subjects had T3 TZ and in 45% of the patients, squamo-columnar junction was completely invisible. The visible transformation zone on the ectocervix was abnormal in 95% patients with 75% patients having grade 1 changes and 17.5% patients having grade 2 changes.

**Table 3: Visibility of squamocolumnar junction on endocervicoscopy**

Visibility of squamocolumnar junction	Number N=40	
	n	(%)
Fully visible	40	(100)
Not visible	0	(0)

The squamocolumnar junction was visible in all the cases. So, the T3 TZ was made fully visible in 100% of the cases.

**Table 4: Findings on endocervicoscopy**

Findings	Number N=40	
	n	(%)
Normal	12	(30.0)
Polyp	10	(25.0)
Polyps with DBV in endocervix	02	(05.0)
Polyp without DBV in endocervix	08	(20.0)
Acetowhite lesions	15	(37.5)
Mild	12	(30.0)

<i>With DBV</i>	03	(07.5)
<i>Without DBV</i>	09	(22.5)
Dense	03	(07.5)
<i>With DBV</i>	02	(05.0)
<i>Without DBV</i>	01	(02.5)
Suspect invasive cancer (Irregular polypoidal mucosa with DBV and dense acetowhitening)	03	(07.5)

DBV-Dilated blood vessels

The findings on endocervicopy were normal in 12 (30%) patients (Fig. 15a). Polyps were seen in 10 (25%) patients. Acetowhite lesions were observed in 15 (37.5%) cases after application of 5% acetic acid. Among these patients, 12 (30%) had mild acetowhitening and 3 (7.5%) patients had dense acetowhitening. Three patients had suspect invasive cancer i.e. irregular polypoidal mucosa with dilated blood vessels and dense acetowhitening. Dilated blood vessels in the endocervical mucosa were seen in 20% (2 out of 10) cases of polyps, 25% (3 out of 12) cases of mild acetowhitening and 66.6% (2 out of 3) cases of dense acetowhitening. Dilated blood vessels were associated with all the cases of suspect invasive cancer.

**Table 5: Histopathology on ECC in women with positive findings on endocervicopy**

Findings on endocervicopy	No. of patients N=28 n (%)	HPE report on ECC					
		Scanty (Inadequate for opinion)	Benign	CIN			Adeno- carcinoma
				I	II	III	
Polyps with or without DBV	10 (35.7)	0	10	0	0	0	0
Acetowhitening	15 (53.5)						
Mild with or without DBV	12 (42.8)	6	6	0	0	0	0
Dense with or without DBV	03 (10.7)	0	1	0	0	1	1
Suspect invasive cancer	03 (10.7)	0	1	0	0	0	2

All 10 polyps were benign on histopathology.

Acetowhitening was observed in 15 patients (53.5%). Twelve (42.8%) patients had mild acetowhitening with or without presence of dilated blood vessels in the endocervical mucosa. Six of these patients had scanty curettings which was inadequate for opinion. Six patients had adequate curettings and were benign in nature.

Dense acetowhitening was seen in 3 patients (10.7%). Out of these 3 cases, one patient had CIN III, second had adenocarcinoma however, third patient had benign histology. She was a treated case of pyometra and endocervical mucosa was inflamed.

Suspect invasive cancer was observed in 3 patients. In 2 of these cases, final histopathological diagnosis was adenocarcinoma and 1 patient had benign histology. She was also a treated case of pyometra with endocervicitis on histopathology.

**Table 6: Work-up of premalignant and malignant cases on HPE (N=4)**

Pap smear	Colposcopic findings	Findings on endocervicoscopy	Diagnosis on ECC and cervical biopsy	Treatment given	Final Diagnosis
HSIL	T3 TZ Grade II acetowhite lesions	Suspect invasive cancer	Adenocarcinoma	Radical hysterectomy	Adenocarcinoma
AGC	T3 TZ Grade II acetowhite lesions	Suspect invasive cancer	Adenocarcinoma	Radical hysterectomy	Adenocarcinoma
HSIL	T3 TZ Grade II acetowhite lesions	Dense acetowhitening with dilated blood vessels	Adenocarcinoma	Radical hysterectomy	Adenocarcinoma
HSIL	T3 TZ Grade II acetowhite lesions	Dense acetowhitening without DBV	CIN-III	LEEP	CIN III

Out of 4 positive cases on histopathology, 3 patients had adenocarcinoma and 1 patient had CIN-III. None of the patients with adenocarcinoma had invasive features on Pap smear or colposcopy. Two patients showed suspect invasive cancer on endocervicoscopy and one patient had dense acetowhitening with dilated blood vessels. Patient with CIN III had abnormal findings on endocervicoscopy in the form of dense acetowhitening without dilated blood vessels.

**Table 7: Predictive values of abnormal endocervicoscopy\***

Findings on endocervicoscopy	N=32 <sup>#</sup> n(%)	Premalignant and malignant lesion on HPE	Benign lesion on HPE
Normal	20 (62.5)	00	20
Abnormal	12 (37.5)	04	08

\*Abnormal endocervicoscopy is defined when there was acetowhite lesion with or without DBV or suspect invasive cancer. Polyps without acetowhitening were not considered abnormal.

<sup>#</sup>Eight patients had scanty curettings and were excluded from the analysis

All 20 patients with normal findings had benign lesion on histopathology. Twelve patients had abnormal findings and 4 out of these had premalignant or malignant pathology.

Positive predictive value (PPV) of the technique for predicting premalignant and malignant lesions was 33.3% and negative predictive value (NPV) was 100%.

**Table 8: Correlation of pap smear, colposcopy and findings on endocervicopy with HPE on cervical biopsy and ECC**

Pap smear	N = 40	Colposcopic findings				Findings on endocervicopy				HPE on cervical biopsy					HPE on ECC			
		Normal	Grade 1	Grade 2	Non-specific	Normal	Polyp	Mild acetowhitening	Dense acetowhitening	Suspicious in invasive cancer	Not sent	Benign	CIN	Malignancy	Scanty	Benign	CIN	Malignancy
NILM	27	2	2	2	1	11	8	7	1	-	1	12	-	-	5	22	-	-
ASCUS	2	-	1	1	-	1	-	1	-	-	-	2	-	-	2	-	-	-
LSIL	5	-	3	2	-	-	2	2	-	1	-	5	-	-	1	4	-	-
HSIL	5	-	2	3	-	-	-	2	2	1	-	2	1	2	-	2	1	2
AGC	1	-	-	1	-	-	-	-	-	1	-	-	-	1	-	-	-	1

The above table gives synopsis of work-up of all the study subjects. Pap smear was normal in 27 patients. Colposcopic findings were normal in 2 patients, grade 1 lesion were seen in 24 patients and non-specific changes i.e. iodine negative uptake was seen in 1 patient. None of the patients with normal pap smear had grade 2 lesions. Findings on endocervicopy were normal in 11 patients and 8 patients had endocervical polyp. Seven of these had mild acetowhitening and 1 had dense acetowhitening. Cervical biopsy was not sent in 15 patients

and remaining 12 patients had benign pathology on cervical biopsy. ECC showed benign pathology in 22 patients and in 5 patients curettings were scanty and inadequate for opinion. Two patients had ASCUS on cytology. Out of these one patient had grade 1 lesion and another had grade 2 lesions on colposcopy. Endocervicopy showed normal finding in 1 patient and mild acetowhitening in second patient. Cervical biopsy revealed benign pathology in both cases. Curettings of both these patients were inadequate for opinion.

LSIL was seen in 5 patients on Pap smear. On colposcopy, 3 patients had grade 1 changes and 2 patients had grade 2 changes. Endocervicopy findings revealed endocervical polyp in 2 patients and mild acetowhitening in 2 patients. Suspect invasive cancer was seen in one patient who was a treated case of pyometra. All these subjects had benign pathology on cervical biopsy. ECC showed benign pathology in 4 patients and was scanty in remaining 1 patient.

Five patients had HSIL on Pap smear. Grade 1 changes on colposcopy was seen in 2 cases and grade 2 changes in 3 cases. On endocervicopy, 2 patients had mild acetowhitening, 2 patients had dense acetowhitening and suspect invasive lesion was seen in 1 patient. Cervical biopsy showed benign pathology in 2 cases, CIN in 1 case and malignancy in 2 cases. ECC revealed benign pathology in 2 patients, CIN in 1 patient and malignancy in 2 patients.

One patient having AGC on cytology showed grade 2 changes on colposcopy. She had suspect invasive cancer on endocervicopy. ECC showed malignancy on histology which was confirmed on cervical biopsy which also came out to be malignant.

## Discussion

In the above study, patient profile revealed the mean age of  $47.23 \pm 11.32$  years. These observations are in agreement with various previous studies. **Autier P et al.**<sup>8</sup> in 1996 found out that the percentage of women having the transformation zone on the exo-cervix decreases with age. He also proposed that with increase in number of live births, the transformation zone is directly exposed to external agents resulting in dysplasia.

On colposcopic examination, all patients had adequate colposcopy with T3 TZ i.e. upper margin of TZ was inside the endocervical canal. Of the 40 patients, SCJ was partially visible in 55% and completely invisible in 45%. Colposcopic findings of the visible TZ on ectocervix were normal in 2 patients. Remaining 38 patients had abnormal findings out of which 30 patients had grade 1 lesion, 7 patients had grade 2 lesions and 1 patient had non-specific changes. In above study, all the subjects were subjected to endocervicopy with office hysteroscope (4 mm) and it was feasible in every case. Majority (70%) of the cases underwent the technique under paracervical block. In cases where associated hysteroscopy was also done, regional or general anaesthesia was used. The procedure was well accepted by the patients under local anaesthesia and only 30% of the patients experienced mild discomfort and pain during the procedure more while taking endocervical curettings. **Bifulco et al.**<sup>7</sup> in 2010 performed endocervicopy with 4 mm office hysteroscope in all patients without any pharmacological premedication or local anaesthesia. However, 8 patients in their study required local anaesthesia to reduce the discomfort during endocervical sampling<sup>14</sup>.

By the technique of endocervicopy, we were able to visualize the complete SCJ in all the cases making the success rate 100% which was the primary objective of our study. However,



it was not possible to delineate the SCJ (360°) at one particular time. At a time only a quarter of SCJ could be made visible.

The idea of using office hysteroscope and 5% acetic acid to visualize the SCJ in T3 TZ is a new concept which was introduced by **Bifulco et al.**<sup>7</sup> in 2010. They used this technique in young women with high grade squamous intraepithelial lesions. They were able to precisely locate the lesion and tailor the length of cone thereby preserving the future fertility in these women. However, no mention has been made in their study about the percentage of complete visibility of SCJ.

**Sharma R et al.**<sup>9</sup> in 1995 used microcolpohysteroscopy in 45 patients with dysplasia. The technique was able to evaluate the endocervical squamocolumnar junction in all cases of unsatisfactory colposcopy rendering the success rate to be 100%. However, the procedure requires expertise and costly instruments limiting the use of the technique.

**Valli F et al.**<sup>10</sup> in 2013 used cervicoscopy and microcolposcopy with waterman blue dye in 119 patients of LSIL and negative or unsatisfactory colposcopy. They reported the visualisation of squamocolumnar junction in 115 (96.6%) patients. In 4 patients (3.4%) the SCJ visualization was not possible because of stenosis of cervical os due to previous cervical surgery. In our study there was no patient with previous cervical surgery and we could achieve complete visualisation of SCJ in 100% of cases.

In above study 12 patients (30%) had normal findings with no suspected lesion and endocervical polyps were identified in 10 (25%) cases. Acetowhitening was observed in 15 (37.5%) patients and suspect invasive cancer in 3 (7.5%) patients. However, we did not find jump lesions in any case. **Bifulco et al.**<sup>7</sup> reported three jump lesions in their study. This could be due to the fact that majority of their study population were HSIL on cytology and the number of cases were also double than ours.

All the patients having normal findings on endocervicoscopy and adequate curettings had benign lesions on histopathology. All polyps showed benign pathology. None of the patients with mild acetowhitening revealed any premalignant or malignant lesion on histology. All patients with premalignant or malignant lesion on final histopathology (adenocarcinoma in three patients and CIN III in one patient) showed dense acetowhitening and irregular polypoidal mucosa on endocervicoscopy. Occurrence of dilated blood vessels was not predictive of malignancy. These were significant when associated with dense acetowhitening or irregular polypoidal endocervical mucosa.

The positive predictive value (PPV) of endocervicoscopy in our study was 33.3% and negative predictive value (NPV) was 100%. This was in contrast to the study done by **Bifulco et al.**<sup>7</sup> who reported the PPV to be 99% and NPV to be 51%. This difference could be due to the fact that in our study, the final histopathological diagnosis was based on the results of endocervical curetting's which has high false negative rates<sup>23</sup>. Whereas, **Bifulco et al.**<sup>7</sup> used the cone biopsy specimen for the final histology report that is more sensitive in predicting premalignant or malignant lesions. We observed that abnormal findings on endocervicoscopy consisting of dense acetowhitening / irregular polypoidal endocervical mucosa with dilated blood vessels were significant in predicting the premalignant and malignant lesions with PPV of 67% and NPV of 100%. It is noteworthy that none of the cases of adenocarcinoma had invasive features on Pap smear and colposcopy and they were diagnosed by abnormal

findings on endocervicoscopy. Mild acetowhitening did not reveal any malignant or its precursor lesions on histopathology thereby indicating that it is an insignificant finding.

The above study shows that endocervicoscopy with office hysteroscope appears to be safe, effective and feasible technique for visualisation of complete SCJ in women with T3 TZ. It has the advantage of delineating the complete morphology of the endocervical canal and precisely localizing any abnormal lesions which get missed on colposcopy in women with T3 TZ. We strongly recommend the use of this technique in cases of T3 TZ which are refractory to other means.

### Conclusion

Endocervicoscopy was found to be 100% successful in visualization of the SCJ in all the cases. However, at a time, only a quarter of SCJ was visible and we had to rotate the office hysteroscope along with the light cable to visualize the SCJ in its entire path. So we recommend that the hysteroscope should be moved to and fro to obtain the complete visualization of the canal. The positive predictive value (PPV) of endocervicoscopy in our study was 33.3% and negative predictive value (NPV) was 100%. The PPV of our study was low as the final diagnosis was based on the histopathological report on ECC. So, we recommend that cone biopsy specimen should be considered for final histopathological diagnosis. Though invasive, endocervicoscopy with office hysteroscope is safe, effective and feasible technique for visualization of squamocolumnar junction in cases of T3 TZ on colposcopy. The above study strongly recommends the use of endocervicoscopy in cases of T3 TZ on colposcopy.

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