

Histopathological and Colposcopic Correlation for Cervical Lesions at Tertiary Care Centre in Central Part of India

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Abstract: ***Objectives:** Aim of the present study is to detect the role of colposcopy and cytology in early detection cervical lesions (benign and malignant) with following objectives: 1. Clinical study of benign and malignant cervical lesions. 2. To differentiate between benign and malignant cervical lesions. 3. To study the correlation of colposcopic appearance with histopathology. **Methods:** It was Hospital based, short term, prospective study. This study was carried out at Bhandari Hospital and Research Centre and Associated Hospitals, Indore, patients attending OPD of Obstetric and Gynaecology department and undergone for colposcopy and cytology of cervix from November 2012 to October 2014. **Results:** In present study 225 patients were included; out of them 45.33% patients were in age group of 30-40 years. Majority of patient 44 % were illiterate. 53.33% patients had first sexual intercourse before 15 years of age. Most common complaint was discharge per vaginum followed by pain in lower abdomen. Colposcopy and colposcopy directed biopsy done accordingly and correlation made. For CIN-1 correlation was 66.67%, for CIN-2 it was 85.71% and for CIN -3 and invasive cancer it was 100 %. **Conclusions:** Colposcopic directed biopsy is considered as Gold standard method for confirmation of cervical intra-epithelial lesions. High grade lesions can be diagnosed by colposcopy more specifically most common drawback associated with colposcopy is over interpretation of the low grade lesions and over treatment because majority of these lesions regress spontaneously over the course of time and during follow up or with treatment. Therefore, combined approach (Pap smear, Colposcopy, Biopsy under colposcopic guidance) is recommended for the evaluation of suspicious cervical lesions and manage accordingly. Fortunately Cervical Cancer has long Pre-invasive phase and with the help of screening methods, Cervical lesions can be diagnosed early and mortality can be reduced or prevented. With recent advances and improvement in screening methods and improved awareness regarding cervical cancer, burden of the disease has been decreased in past few decades.*

Keywords: Colposcopy, CIN, HSIL, Cervical Lesion.

1. Introduction

“Women are primary care-taker in family and backbone of society. Any health problem (physical, mental and social) of women directly affects the family as well as society. Any early death of women in family, make family like a house without roof. “

Cervical cancer is one of the commonest cause of cancer-related deaths among women, and indicates health inequities.^[1] Majority of deaths because of cervical cancer (86%) happen in developing, low- and middle-income countries.^[1]

Around the globe 528, 000 new cases of Cervical Cancer were detected and 266, 000 deaths were reported because of Cervical Cancer.^[2] Human Papillomavirus (HPV) is main Causitive agent for cervical cancer^[3]. Cervical cancer follow distinctive pre-cancerous condition that is called as Cervical Intraepithelial Neoplasia (CIN).^[4] Very recent trend is to use term squamous intra-epithelial lesion (SIL). Depending upon the severity of the lesion (CIN I, CIN II or CIN III) it can progress to become cancer cervix, if not treated timely. Screening methods are considered as secondary prevention that includes early diagnosis of disease (at pre cancerous conditions).^[5] Cytological methods of screening (Pap smear and liquid base cytology) are used all over the world, cytological methods have sensitivity ranges from 44-78% and specificity 91-96% for developing countries, and have achievements in reducing mortality because of cervical cancer particularly, over developed world.^[5] Nationwide screening program is mandatory^[1] to avoid disparities in screening, treatment as well as survival. Population based survey^[1] reported that coverage of cervical cancer screening

was low (19%) in developing countries when compared with developed countries (63%). Screening methods are not used by older and poor women routinely, and they are at highest risk to develop cervical cancer. Opportunistic screening for cervical cancer varied from different part of India. It was 6.9% in Kerala^[1] and 0.002% in south part of Tamilnadu.^[1] Most of the cervical cancer cases are diagnosed at advanced stage leading to more mortality, morbidity and more expenditure.^[1] So it is the best exercise to implement cervical cancer screening programme nation wide to achieve healthy life. And make cancer free nation.

Now-a-days HPV DNA (High risk type) is considered as a important screening test of cervical cancer. It has better predictive value, if it is negative there is low risk of developing cervical cancer than negative pap smear,^[6] because it has high negative predictive value.^[6]

Specificity of colposcopy increases as severity of the lesion increases. So it is better to use both (cytology and colposcopy) for diagnosis of cervical pre-malignant and malignant lesions as they are complementary to each other.^[7]

The main objective^[1] of cervical cancer screening is to detect the cervical lesions at earlier stage (pre-cancerous condition) and managed accordingly to prevent development of invasive cervical lesion. Important components^[1] of the screening program are acceptable, affordable, prompt diagnostic investigations, adequate treatment and proper follow up after treatment. Success of screening program mainly depends upon high level of participation, health care infrastructure and availability of human resources.^[1]

Present study is undertaken with the aim of detection of cervical malignancy at earlier stage so that mortality and morbidity can be reduced. Screening methods selected are Colposcopy along with Cytology because cytology has high specificity and colposcopy has high sensitivity and high specificity for detection of cervical lesions.

2. Methods

It was Hospital based, short term, prospective study. This study was carried out at Bhandari Hospital and Research Centre and Associated Hospitals, Indore, patients attending OPD of Obstetric and Gynaecology department and undergone for colposcopy and cytology of cervix from November 2012 to October 2014.

The sample size taken is based on the literature reviewed of the authors who had done the work on similar topic. The sample size was not calculated, prior to initiation of the study, but with the present sample size taken for the study, the power of the study was calculated that was more than 80%. So, the sample size is justified.

Selection of Cases

Inclusion Criteria:

- 1) Abnormal appearance/suspicious looking of cervix
- 2) Abnormal PAP smear
- 3) White discharge per vaginal (persistent and undiagnosed blood mixed).
- 4) Menstrual abnormalities e.g. post menopausal bleeding, intermenstrual bleeding and post coital bleeding.
- 5) Asymptomatic cases with routine PAP smear
- 6) High risk patients for cancer cervix
- 7) Sexually transmitted diseases

Exclusion criteria:

- 1) Pregnant patients

3. Methodology

Relevant history was taken and clinical examination was done, Procedure explained to patients and informed consent was obtained. Pap smear was taken. The cervix is examine through colposcope, first in low power and then under higher magnifications. Finally green filter is used to identify the vascular pattern. 5% acetic acid was applied over the cervix and acetowhiteness was studied with respect to color, surface, and margins etc. Colposcopy is termed satisfactory, when squamocolumnar junction was completely visible and borders of all lesions are well defined. Lugol's Iodine was applied and iodine negative area were examined.

A biopsy was taken from suspicious areas under colposcopic guidance and sent for histopathological examinations. Haemostasis was achieved with Silver nitrate solution application locally at the site of biopsy taken. Documentation of Colposcopic findings were made and explained to the patient in post procedure counseling. Patient was advised to consult immediately in case complications such as fever, bleeding, pain or foul smelling discharge occurs.

Financial Inputs and Funding

No additional procedures/ tests were performed specifically for the need of the research. Hence, there was no financial burden either on the institution or on the patients.

Ethical Considerations

The protocol of the present study was submitted to the Research Committee of Bhandari Hospital & Research Centre, Indore. Study was initiated after getting written approval from the committee the in the institution.

4. Results

In present study 225 patients were included and following observations were made.

Table 1: Demographic profile of patients

		No. of Patients	Percentage
1. Age	20-30 years	69	30.67
	31-40	102	45.33
	41-50	42	18.67
	>50	12	5.33
2. Residence	Rural	153	68
	Urban	72	32
3. Literacy	Educated	126	56
	Uneducated	99	44
4. Age at First Coitus	<15years	120	53.33
	16-20	96	42.67
	>20	09	04.00
5. Parity	Nullipara	6	2.67
	Para 1	15	6.67
	Para 2	57	25.33
	>3	147	65.33
6. Contraception	Users	48	21.33
	Nonusers	177	78.67

Table 2: Distribution of Patients as per Clinical Complaints

Complains	Number of Patients	Percentage
Discharge PV	189	84.00
Pain in abdomen	90	40.00
Backache	42	18.67
Irregular menses	36	16.00
Menorrhagia	30	13.33
Itching in private parts	24	10.67
Burning micturition	18	8.00
Dyspareunia	12	5.33
Post coital bleeding	6	2.67

Table 3: Distribution of Patients According to Per Speculum Finding

Per Speculum Findings	Number of Patients	Percentage
Discharge	186	82.67
Cervical erosion	120	53.33
Ectropion	108	48.00
Vaginitis	57	25.33
Cystocele	42	18.67
Rectocele	27	12.00
Irregular cervix	21	9.33
Bleeds on touch	9	4.00
Polyp visible	3	1.33

Table 4: Correlation of Colposcopic Findings to Histopathology

HPR	Normal		Benign		CIN I		CIN2		CIN III		Invasive Carcinoma	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Not done	12		75									
Atrophic cervicitis	0	0	3	2.78	3	4.17	0	0.00	0	0.00	0	0.00
Chronic cervicitis	0	0	12	11.11	9	12.50	0	0.00	0	0.00	0	0.00
TB cervicitis	0	0	3	2.78	0	0.00	0	0.00	0	0.00	0	0.00
Squamous metaplasia	0	0	6	5.56	12	16.67	0	0.00	0	0.00	0	0.00
Leukoplakia	0	0	3	2.78	0	0.00	0	0.00	0	0.00	0	0.00
Endocervical polyp	0	0	3	2.78	0	0.00	0	0.00	0	0.00	0	0.00
Leiomyomatous polyp	0	0	3	2.78	0	0.00	0	0.00	0	0.00	0	0.00
CIN-1	0	0	0	0.00	48	66.67	3	14.29	0	0.00	0	0.00
CIN-2	0	0	0	0.00	0	0.00	18	85.71	0	0.00	0	0.00
CIN-3	0	0	0	0.00	0	0.00	0	0.00	9	100.00	0	0.00
Invasive carcinoma	0	0	0	0.00	0	0.00	0	0.00	0	0.00	3	100.00
Total	12	0	108	100.00	72	100.00	21	100.00	9	100.00	3	100.00

Chi square value = 159.77 at 20 df with probability of 0.000 Highly significant

Table 1 shows that 45.33% of the patients were in age group 30-40 years. The mean of age is 36 years & 68% of the population in our study belonged to rural area. Majority of population in our study were illiterate 44%. This table also shows that 53.33% patients were married early and had history of sexual intercourse at < 15 years of age and 42.67% had sexual intercourse between 16-20 years and small number (4%) of population had sexual intercourse between 21-25 years of age group & 65.33% of population were para 3 or more and only 2.67% were nullipara. It also shows that 78.67% of the population in our study did not use any type of contraception.

Table 2 shows that the most common clinical complaint in our patients were discharge PV in 84% of patients either alone or in combination with other symptoms. Pain in abdomen was the next commonest presenting complaint (40%). Table 3 shows that the most common per speculum finding in our patient was cervical erosion in 53.33%, discharge PV was seen in 82.67% of cases, either in association with erosion or alone.

Table 4 shows that out of 72 cases colposcopically detected as CIN I, 48 (66.67%) were histopathologically detected as CIN I. While out of 21 cases colposcopically detected as CIN II 18 (85.71%) were histopathologically detected as CIN II and complete 100% correlation of colposcopy and histopathology in detecting CIN III and invasive cancer.

5. Discussion

The present study was carried out at Bhandari Hospital and Research Centre and Associated Hospitals, Indore, patients attending OPD of Obstetric and Gynaecology department and undergone for colposcopy and cytology of cervix. In present study 225 patients were included and following important factors studied in detail.

Influence of Age

The cases included in our study belonged to age group 20-60 years, and 36 years age was found as mean age for studied population. In a study that was undertaken by **Bharti et al**^[8] (October 2002 to December 2004) evolved 380 patients in the age group of 30-60 years (mean 39.48 ± 8.91 years). Another study was carried out by **Thakre et al**^[9] also found more than half (62.5%) of the studied population

belonged to the age group of 31-50 years. In present study, we observed that as age advances, severity of the disease increases. Cervical pre-invasive lesions (CIN I, CIN II and CIN III) were predominantly found in age group 30-40 years. Majority of (more than 50%) CIN I / CIN II cases and 33% of CIN III cases belonged to age group 30-40 years. While invasive lesions predominantly found in age more than 40 years. Satisfactory colposcopy was present with mean age of patient was 32 years. And pre-invasive lesions (CIN I, CIN II and CIN III) were diagnosed at younger age group (for CIN I, age 30 years and for CIN II, CIN III, age 32 years).

Case-control study was conducted by **Hildesheim et al**,^[10] within a population-based cohort of 10 077 women in Costa Rica. They found that cancer cases were older than HSIL cases. Median age for cancer = 47 years vs. median age for HSIL = 34 years, respectively. Median age for the LSIL = 29 years vs. 32 years for the HPV positive only group. While CIN2 cases were younger than CIN3/cancer cases (median age for CIN2 = 31 and median age CIN3/cancer = 38, respectively), HSIL/CA cases were, on average, 4 years older than controls (median age = 36 for HSIL/CA and 32 for LSIL/HPV).

Influence of Rural Inhabitation and Literacy

In the present study we found that majority of patients (68%) belonged to rural inhabitation and illiteracy was present in 44% of total population studied. A study was conducted by **Franceschi et al 2001**.^[11] They found that Illiteracy (OR vs. high education 4.8), lack of a toilet (OR 4.8) were significantly associated with ICC (Invasive Cervical Cancer) risk. Another study was conducted by **Rajput et al**^[12] they found histopathological interpretation of Pap's smear revealed cervical squamous epithelial disease (LSIL and HSIL) in 10.5% smears of rural and 4.5% smears of urban women. A total of 4% smears were found positive for malignancy in rural women when compared to 1.5% smears in urban women.

Influence of Age at Marriage and Consummation of Marriage

In present study, we found that, longer exposure of sexual activity and younger age at first sexual activity was significantly associated with pre-invasive and invasive lesions of cervix. Mean age at marriage was 15.22 years in

present study. Early ages at marriage and early onset of sexual activity (at younger age) were significantly associated with cervical pre-invasive and invasive lesions. In our study we found that, 54.17% of CIN I cases, 57.14% of CIN II, 66.67 % of CIN III cases and 100% of invasive lesions were present in patients with early started sexual activity (before 15 years of the age). A study was conducted by **Franceschi et al**^[11] they found that Age at first intercourse <15 years (OR vs. ≥ 21 years = 2.2) significantly associated with risk of invasive cervical cancer. Another study carried out by **Thakre et al**^[9] included 200 married women in their study, and they had conclusion that 87.5% appellants got married before the age of 18 years, 60.61% had their first child before the age of 18 years.

Influence of Parity

In the present study, we found that mean parity of studied population was 3, severity of the disease increases with increasing parity we found that 66.67% of total CIN I cases, 100% of total CIN II cases and 66.67% of total CIN III cases were found to be parity more than or equal to 3.

Case-control study conducted by **Hildesheim et al**,^[10] within a population-based cohort of 10 077 women in Costa Rica In those women with a high-risk HPV type infection, 42% of HSIL/Carcinoma (95% CI = 21 to 63 years) can be attributed to multiparity

Influence of Contraception

In the present study, we found that majority of (78.67%) of studied population did not use any method of contraception and spacing methods were used only by 21.33% of studied population. In present study we found that out of 7 cases of Cu-T users, 1 had CIN I, 4 had CIN II and 2 had CIN III on colposcopy. In our study OCP user were minimum so we have not found any significant association between OCP use and preinvasive and invasive lesion of cervix.

A study was conducted by **Rajput et al**^[12] they had result that barrier methods were used by rural women only 12% while in urban areas users were 30%.

Correlation of Clinical Complaints and Findings on Per Speculum Examination

In the present study we found that most common (84%) clinical complaint was white discharge per vaginum and on per speculum examination it was present in 82.67% patients and cervical erosion was found in 53.33% patients.

A prospective observational study was conducted by **Chaudhary et al**^[13] and they found that White discharge per vaginum was the most common complaint followed by pelvic pain in 39 % cases. On per speculum examination, cervical erosion was the most common clinical presentation in 86.5% cases.

Correlation of Colposcopy and Histopathology

In the present study we found that the accuracy of colposcopy for the diagnosis of cervical lesion increases as the severity of the disease increases. When colposcopic findings were correlated with histopathology we found that correlation was 66.67% 85.71% and 100% for CIN I, CIN II

and CIN III/invasive cancer respectively. In present study we found that sensitivity and specificity of colposcopy for CIN I was 66.6% and 98% respectively for CIN II was 85.7% and 100% and for CIN III was 100% and 100% respectively. In our study we found that accuracy of colposcopy in picking up high grade lesions is high.

A prospective observational study was conducted by **Chaudhary et al**^[13] they found that sensitivity of colposcopy was 79.37%, specificity 81.02%, positive predictive value (PPV) 65.79%, negative predictive value (NPV) 89.52% respectively and accuracy was 80.5%. p-value P<0.0001, Significant. Sensitivity for detection of cervical cancer is high.

6. Conclusion

Dysplasia and invasive cervical cancers can be diagnosed early with colposcopy, as modern colposcopy has high sensitivity and specificity. Colposcopy can be considered as a intermediate link between cytology and histopathology. Colposcopic directed biopsy is considered as Gold standard method for confirmation of cervical intra-epithelial lesions. High grade lesions can be diagnosed by colposcopy more specifically most common drawback associated with colposcopy is over interpretation of the low grade lesions and over treatment because majority of these lesions regress spontaneously over the course of time and during follow up or with treatment. Therefore, combined approach (Pap smear, Colposcopy, Biopsy under colposcopic guidance) is recommended for the evaluation of suspicious cervical lesions and manage accordingly.

Fortunately Cervical Cancer has long Pre-invasive phase and with the help of screening methods, Cervical lesions can be diagnosed early and mortality can be reduced or prevented. With recent advances and improvement in screening methods and improved awareness regarding cervical cancer, burden of the disease has been decreased in past few decades.

Cervical cancer screening methods must be applied according to guidelines to make society free from cervical cancer as it is preventable.

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