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Study of colposcopic and histopathological correlation for cervical lesion at tertiary care: An original research

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***Abstract*---**Introduction–Colposcopy is the diagnostic method for cervical cancer. It involves visualization and examination of cervix, vagina and vulva with the aid of a colposcope. Similar to pap smear, colposcopy is also a non-invasive method but is expensive and thus it is used as typically to assess the presence, location, size, extent, as well as type of pre-cancer or cancer. Also, it is helpful in guiding the appropriate site for taking the biopsy for histopathological examination.Objective- To study the colposcopic findings of cervical lesions in patients and to differentiate between benign and malignant cervical lesions. Also, correlating the colposcopic findings with histopathological findings. Material and methods- The present study entitled "Study of Colposcopic and Histopathological Correlation for Cervical Lesions at Tertiary Care Centre" was conducted in Department of Obstetrics and Gynecology on a total of 250 females. Data was compiled and correlation between the findings of colposcopy and histopathology was done. Level of agreement between colposcopic and histopathologic findings was calculated using kappa statistics. P

value <0.05 was considered significant. Result- Colposcopy correlated with histopathology for 47.2% cases of cervicitis, 32% CIN I, 41.7% CIN II and 36.4% CIN III. Diagnostic accuracy, sensitivity, specificity, PPV and NPV was 77.2%, 78.6%, 76.1%, 72.7% and 81.4% respectively. Conclusion-Colposcopy can be used reliably as a screening method among women presenting with various lesions of cervix colposcopy showed good correlation with histopathology for identification of premalignant lesions and may obviate the need for repeated pap smear.

***Keywords*---**Cervical Lesions, histopathology for identification, Colposcopy correlated.

Introduction

Cervical cancer, a major public health problem worldwide is a preventable disease. Cervical cancer is the fourth common cause of cancer globally whereas in India, it is second most common cause of cancer among females.[1] The etiology of cervical cancer is mainly attributed to Human papilloma virus. According to HPV information Centre India, approximately 83.2% invasive cervical cancer are due to HPV 16,18 while 5% women harbour HPV 16,18.[2] **World Health Organization** estimated approximately 5,70,000 new cases globally in 2018 attributing to approximately 12-15% of all cancers among women, however, crude incidence of cervical cancer in females in India have been estimated to be 14.9% by HPV centre.[2,3] The new cases registered during the year of 2018 were 96222 women with median age of38 years (age 21–67 years) and deaths were observed in 60078 females according to a report of **Globacan** (2018).[4] The age standardized incidence rates of cervical cancer is also higher in India (22 per 100000 women year) as compared to 19.2, 13 and 2.8 per 100000 women per year in Bangladesh, Srilanka and Iran respectively.[1] The higher incidence as well as mortality in India have been attributed to certain risk factors such as low socioeconomic status, marriage before age of 18 years, young age at first coitus, high parity, poor genital hygiene, malnutrition, use of oral contraceptives, and lack of awareness. Other risk factors attributed to cervical cancer include smoking and multiple sexual partners.[5] Cervical cancer has long preinvasive stage, which progress from mild dysplasia to carcinoma in situ to frank carcinoma over 10 to 20 years. Thus, this cancer is preventable and is amenable to detection by screening methods during early preinvasive stage.[6] Timing of diagnosis and extent of disease at the time of diagnosis determine the prognosis in cases of cervical cancer. Early diagnosis and management are associated with less intensive treatment, good outcome and reduced morbidity and mortality. Thus, screening methods must be employed for detection of lesions during the early premalignant stage at which the disease is still reversible.[7] WHO recommend three methods for screening of cervical cancer viz. PAP smear, visual inspection with acetic acid and HPV DNA testing.[3] In high income countries, screening alone with Pap test have significantly reduced morbidity as well as mortality associated with cervical cancer, however, in low middle income counties like India, the coverage of screening is much low probably

due to low level of awareness among the beneficiaries. Also due to high population and lack of resources, it is difficult to reach the population through cytology-based screening programme. Thus, patients are subjected to screening after the onset of symptoms.[8] Pap smear test is the most common primary screening method which help in detection of cervical epithelial changes during preinvasive or early invasive stages. [9,10] This method of screening is non-invasive, safe, simple, and can be done on OPD basis without requiring admission. The conventional method of Pap smear test has high false negative rate (approximately 10 to 70%) which is attributed to collection and processing errors.[11] Colposcopy is the diagnostic method for cervical cancer. It involves visualization and examination of cervix, vagina and vulva with the aid of a colposcope. It is a unique which help in assessment of both benign as well as premalignant lesions. Similar to pap smear, colposcopy is also a non-invasive method but is expensive and thus it is used as typically to assess the presence, location, size, extent, as well as type of pre-cancer or cancer. Also it is helpful in guiding the appropriate site for taking the biopsy for histopathological examination.[12]Colposcopy alone has sensitivity of 60 to 75% for detection of cervical intraepithelial neoplasia whereas when combined with exfoliative cytology, sensitivity has been reported to increase to more than 90%.[13] Histopathological examination is a gold standard technique for identification of cervical cancer but it is an invasive technique.[14]It reveal the degree of abnormality in cervical epithelial cells and confirm or refute the diagnosis of cancer. Histopathology helps in classification of cells of cervix as normal, dysplastic, neoplastic.[12] Diagnostic algorithm of screening program include screening with pap smear followed by colposcopy and confirmation by histopathology.[15] Correlation between cytological, colposcopic and histopathological findings is important way of assurance of internal quality. Such correlation also helps to assess the factors associated with variable findings. With the above background, the present study was conducted at tertiary care centre to study the colposcopic and histopathological findings of cervical lesions and to correlate between the findings of colposcopy and histopathology.

Aims and Objectives:

To study the colposcopic findings of cervical lesions in patients. To differentiate between benign and malignant cervical lesions. To correlate the colposcopic findings with histopathological findings.

Materials and Methods:

The present study entitled “Study of colposcopic and histopathological correlation for cervical lesions at tertiary care centre” was conducted at Department of Obstetrics and Gynaecology. All the outpatient and inpatient females in the age range of more than 20 years presenting at study area with white discharge, menstrual abnormalities, abnormal looking cervix, via positive, sexually transmitted diseases, with abnormal pap smear. Sample size was 250. Inclusion criteria- All females with Abnormal appearance/suspicious looking of cervix, VIA Positive, Abnormal PAP smear, White discharge per vaginal (persistent and undiagnosed blood mixed), Menstrual abnormalities

e.g., post-menopausal bleeding, intermenstrual bleeding and post coital bleeding. High risk patients for cancer cervix. Sexually transmitted diseases. Exclusion criteria: Pregnant females. Detailed data regarding family history, menstrual history, parity, history of risk factors, sexual history and sexually transmitted diseases was obtained. Their clinical, per speculum, per vagina examination was done. All patients were subjected to routine and special investigations such as CBC, LFT, RFT, thyroid profile, RBS, HIV, HBsAg, VDRL, urine analysis and vaginal swab routine and culture sensitivity. Patients who were symptomatic and with abnormal cervix, with VIA positive, abnormal PAP Smear further counselled for examination and testing and were subjected to colposcopy and biopsy of cervical lesions. The procedure for conducting colposcopy was as follows: Patient was put in lithotomy position, the largest size Graves speculum, which the patient could tolerate, was inserted, taking care not to injure the cervix. Initially an unaided visual inspection of the cervix was performed under good illumination and findings were noted. Cervix will be examined with 12-15X magnification without application of acetic acid for presence of obvious growth, leukoplakia and abnormal vascular pattern. Vascular pattern was further evaluated using a green filter. Subsequently 5% acetic acid was applied on the cervix and any resultant change in cervical epithelium was noted. In the presence of any abnormal finding on colposcopy, a directed biopsy was obtained first from the posterior lip and then if required from the anterior lip using a punch biopsy forceps. Bleeding from the biopsy site was controlled by pressure. Findings were noted and all lesions (benign and malignant) were classified according to IFCPC Classification 2011. Adequacy and inadequacy of the squamocolumnar junction was noted as transformation zone T-1, T-2, T-3.[17]. Modified Reid's Colposcopic index was calculated. Biopsy taken and sent for histopathological examination. Histopathology reports were collected. Correlation of colposcopic findings with histopathological findings was done and level of significance was calculated.

Data obtained was compiled and grouped. Grouped data was expressed as frequency and percentage whereas numerical data was expressed as mean and standard deviation. Correlation between the findings of colposcopy and histopathology was done. Sensitivity, specificity, diagnostic accuracy, positive predictive value, negative predictive value of coloposcopy was calculated against histopathology and expressed as percentages. Level of agreement between colposcopic and histopathologic findings was calculated using kappa statistics. P value <0.05 was considered significant.

Results:

Mean age of females was 36.89±8.9 years and majority of females in present study belonged to 26 to 35 years of age group (43.6%), followed by 33.2% and 13.6% females in the age range of 36 to 45 and 46 to 55 years respectively. Only 2.4% females belonged to more than 55 years of age group. About 57.6% females were resident of urban areas in present study whereas only 42.4% females resided in rural areas. Majority of patients in our study were house wives 144 (57.6%) whereas 41 (16.4%) were labourer respectively. Majority of husbands of females in our study were driver (50%), whereas about 34% and 14% were daily workers and

were engaged in service respectively. Maximum females were illiterate (49.6%) followed by 31.6% females educated up to primary school. Only 1.6% females achieved higher secondary level of education. Modified Kuppuswamy scale was used to assess socioeconomic status of patients. Based on this scale, majority of females belonged to upper lower socioeconomic status (49.2%) followed by 46% females in lower middle socioeconomic status. Only 0.4% females belonged to upper middle socioeconomic status and none of the females in our study belonged to upper socioeconomic class. For maximum i.e., 62% females, age at marriage ranged between 18 and 29 years. However, late marriage i.e., after 30 years was documented in 32% cases and early marriage was noted in 6% females. Age at first intercourse was documented to be $\leq$ 20 years in 63.2% females whereas it was $\geq$21 years in 36.8% cases. High risk history i.e., history of multiple sexual partners was observed in 0.8% females in present study. Any form of contraceptive use was noted in 40.8% females. Majority of females underwent permanent sterilization procedure (18.4%), however, 8% females used copper T. About 7.2% cases used OCP and Barrier methods of contraception each. Maximum females were para 2 and para 3 (29.2% and 25.2% respectively). Only 0.8% females who were screened were nulliparous. In present study, maximum females presented with more than one symptom. Most common mode of presentation was discharge per vagina noted in 58.8% females followed by chronic pain in lower abdomen observed in 48% females. Post coital bleeding and dyspareunia were least commonly documented symptom in 2.4% and 2% females respectively. However, no associated symptoms were documented in 3.6% females. Per speculum examination revealed hypertrophied cervix in majority i.e., 64% of females followed by cervical ectropion, discharge and hypertrophied cervix with nabothian cyst in 40%, 22% and 8.4% cases respectively. However, in about 6.8% females, per speculum examination revealed normal findings. Modified Reid's colposcopic index ranged between 0 to 2 in majority of cases (62%), whereas in 24.8% and 13.2%, Modified Reid's index ranged between 2 to 4 and 5 to 8 respectively. Colposcopy revealed miscellaneous inflammation in 32% cases followed by faint Acetowhite lesions with fine punctations or mosaicism (grade 1 minor) in 14.8% cases, and non-specific erosion in 10.8% cases. Apart from this, Dense acetowhite lesions with coarse punctations or mosaicism with partial iodine uptake (GRADE 2 MAJOR) was noted in 10% cases whereas in 4% cases, colposcopy revealed atypical vessels, irregular surface, exophytic growth, necrosis ulceration tumor suggesting cancerous invasion. However, colposcopy revealed normal findings in 18% cases. In present study, majority of females were diagnosed colposcopically (Table- 1) as having inflammation (32%), followed by CIN I (21.6%), CIN II (16.4%) and CIN III (8%). However, cancer was suspected in 2.4% females and 18% females had normal cervix. Histopathological diagnosis revealed chronic cervicitis as most common feature, with or without other changes (35.6%). However, histopathology (Table- 2) revealed normal findings in 18% females. Mild, moderate and severe dysplastic changes were noted in 20%, 14.4% and 8.8% females in present study respectively. Histopathology was suggestive of squamous cell cancer in 1.6% cases. Out of 89 cases of chronic cervicitis, 47.2% cases were diagnosed as inflammation whereas 22.5% were identified as CIN I on colposcopy. However, 18% chronic cervicitis cases were identified as normal on colposcopy. All the histopathological cases of polyp were diagnosed as polyp on colposcopy. Out of 22 cases of CIN I on histopathology, colposcopy revealed CIN I in 32% cases. Similarly, histopatho-colposcopic

correlation (Table- 3) for CIN II and CIN III cases were noted in 41.7% and 36.4% cases respectively. Out of 4 squamous cell carcinomas, none of the cases were diagnosed as cancer on colposcopy. The observed correlation between histopathology and colposcopy was statistically significant ($p<0.01$). Diagnostic accuracy, sensitivity, specificity, PPV and NPV was 77.2%, 78.6%, 76.1%, 72.7% and 81.4% respectively.

Discussion

Colposcopy is a non-invasive diagnostic procedure that involves visualization and examination of cervix, vagina and vulva with the help of device called colposcope. It is helpful in evaluation of lesions of cervix including benign, premalignant as well as malignant lesions. Colposcopy may also be helpful in guiding site for taking the biopsy for histopathological examination.[12] Though, histopathological examination is gold standard method for accurate diagnosis of cervical lesions, this method is invasive. Correlation between the findings of colposcopy and histopathology is an important way of internal quality assurance. The age composition of patients of present study were concordant to findings of previous studies as shown in table 18. However, majority of patients in a study by **Bindroo S et al (2019)** belonged to higher age group as compared to present study i.e., 41 to 50 years (32%). In present study, majority of patients were house wives (57.6%) whereas about 16.4% were labourer. Similarly, majority of patients in a study by **Almiraw JA et al (2020)** Majority of patients in our study were house wives 144 (57.6%) whereas 41 (16.4%) where labourer respectively were housewives (>60%). However, majority of patients in a study by **Kassa LS et al (2019)** were government employee (35%) followed by housewives. The findings of present study were concordant with findings of **Khatri S et al (2015)**, in which majority of patient i.e., 44% were illiterate. In present study, majority of patients belonged to upper lower (49.2%) and lower middle socioeconomic status (46%) according to modified Kuppuswamy scale. Present study was conducted at tertiary care centre, where people especially from lower socioeconomic strata seek care. These findings were supported by **Olanian OB et al (2002)** in which authored documented definitive role of low socioeconomic status on the development of dyskaryosis.However in a study by **Ramadevi E et al (2017)**, about 80% cases of CIN l and 50% cases of CIN II belonged to lower socioeconomic status. Higher incidence if premalignant cervical lesions in females with low socioeconomic status have been attributed to poor personal hygiene, poor living conditions, unstable marriages and early age at first intercourse. In present study, majority of females (63.2%) gave history of initiation of sexual activity before 20 years of age. Similarly, **Khatri S et al (2015)** also documented that about 53.33% patients had first sexual intercourse before 15 years of age. Long term use of oral contraceptive especially more than 12 years have been associated with excess risk of cervical cancer. The association is somewhat stronger for adenocarcinomas than for squamous cell carcinomas. In our study, contraceptives in the form of oral contraceptive pills were used by 7.2% females only. Also 7.2% females used barrier method of contraception. About 18.4% females gave history of tubectomy. The findings of present study were concordant with findings of **Bhattacharya AK et al (2015)** in which majority of females were parity more

than 2. Also, they documented incidence of CIN and cervical cancer to be higher in females with higher parity. Our study included the females presenting with various lesions of cervix. Maximum females in our study presented with more than one symptom. Most common clinical feature being white discharge per vaginum (58.8%) followed by chronic pain in lower abdomen (48%). Apart from this, post coital bleeding, dyspareunia was also observed in few patients. These findings were concordant with the findings of **Fuke RP et al (2020)** in which most common clinical feature among females with various cervical pathology was persistent vaginal discharge, postcoital bleeding, menstrual abnormalities. **Kaur B et al (2017)** documented discharge per vagina and pain abdomen as most common complaint observed in 94.66% and 92% respectively. Modified Reid Index Score was used for classifying the colposcopic findings. Based upon this score, benign inflammation (Index 0-2) was the most common finding observed in 62% cases whereas in 24.8% and 13.2%, Modified Reid's index ranged between 2 to 4 and 5 to 8 respectively. In present study, gross colposcopic findings showed miscellaneous signs of inflammation in majority of cases i.e. 32% cases. followed by faint Acetowhite lesions with fine punctations or mosaicism (grade 1 minor) in 14.8% cases, and non-specific erosion in 10.8% cases. Based upon gross colposcopic findings, colposcopic diagnosis was made which included inflammation as most common diagnosis (32%), followed by CIN I (21.6%), CIN II (16.4%) and CIN III (8%). However, cancer was suspected in 2.4% females. The findings of present study were concordant with the findings of **Gandavaram J et al (2019)** in which based on the Reid's scoring system, majority of cervical lesions were benign inflammatory (58.4%) followed by 23.25% low grade, 13.6% high grade and 4.8% as carcinoma. Histopathology was suggestive of chronic cervicitis with and without koilocytosis in majority of cases (32%). Polyp was observed in 1.6% cases. Mild, moderate and severe dysplastic changes were noted in 20%, 14.4% and 8.8% females respectively whereas squamous cell cancer was observed in 1.6% cases. However, histopathology revealed normal findings in 18% females. Histopathology correlated with colposcopy for diagnosis of polyp in 100% cases, whereas histopatho-colposcopic correlation for CIN I, II and III was observed in 32%, 41.7% and 36.4% cases respectively. These findings were concordant for premalignant lesions with the findings of previous studies described in table 22. The findings of present study however were in contrast to **Boicea A et al (2012)** [18] in which higher correlation was noted between histopathology and colposcopy as compared to present study.

Conclusion

Lesions of cervix are one of the most common causes for which female of various age seek medical care. Colposcopy is non-invasive screening as well as diagnostic method for various lesions of cervix. Colposcopy can be used reliably as a screening method among women presenting with various lesions of cervix. However, the accuracy of colposcopy is dependent on the training, expertise, and skill of the operator with emphasizes proper training, certification, and experience of colposcopist. Histopathology of suspected lesion remains the gold standard for the final diagnosis of benign and precancerous lesions. However, colposcopy showed good correlation with

histopathology for identification of premalignant lesions and may obviate the need for repeated pap smear. Therefore, combined approach (PAP's Smear, Colposcopy, Biopsy under colposcopic guidance) is recommended for the evaluation of suspicious cervical lesions and manage accordingly. Hence "SINGLE VISIT" Screen and treat strategy can be cost effective as well as time saver which is crucial to bring down the incidence and mortality due to cervical cancer.

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Table 1- Distributions Of Cases According To Colposcopic Diagnosis

Colposcopic diagnosis	**Total no. of cases (n=250)**	**Percentage**
Normal	45	18
Inflammatory	80	32
CIN I	54	21.6
CIN II	41	16.4
CIN III	20	8
Polyp	04	1.6

Suspected cancer	06	2.4

Table 2- Distribution Of Cases According To Histopathology Findings

Histopathological finding	**Total no. of cases=250)**	**Percentage**
Normal	45	18
Chronic cervicitis	80	32
Chronic cervicitis with hyperplastic epithelium with koilocytosis	09	3.6
Polyp	04	1.6
Mild dysplasia with koilocytosis	50	20
Moderate dysplasia with koilocytosis	36	14.4
Severe dysplasia	22	8.8
Squamous cell cancer	04	1.6

Table 3- Correlation Between Colposcopic Diagnostic Findings And Histopathology Findings

Colposcopy	**HISTOPATHOLOGY**							**Total colposcopy**
	Normal	**NSpCC**	**Polyp**	**CIN I**	**CIN II**	**CIN III**	**Carcinoma**	

Normal	26 (57.8)	16 (18)	0 (0)	2 (4)	1 (2.8)	0 (0)	0 (0)	45
Inflammation	17 (37.8)	42 (47.2)	0 (0)	16 (32)	3 (8.3)	0 (0)	2 (50)	80
Polyp	0 (0)	0 (0)	4 (100)	0 (0)	0 (0)	0 (0)	0 (0)	4
CIN I	2 (4.4)	20 (22.5)	0 (0)	16 (32)	10 (27.8)	5 (22.7)	1 (25)	54
CIN II	0 (0)	9 (10.1)	0 (0)	12 (24)	15 (41.7)	5 (22.7)	0 (0)	41
CIN III	0 (0)	2 (2.2)	0 (0)	4 (8)	5 (13.9)	8 (36.4)	1 (25)	20
Suspected cancer	0 (0)	0 (0)	0 (0)	0 (0)	2 (5.6)	4 (18.2)	0 (0)	6
HPR Total	45	89	4	50	36	22	4	250
x^2=421.96; p=0.001								