

# Original Research Paper

Pathology

# HISTOPATHOLOGICAL STUDY OF COLPOSCOPIC BIOPSY OF CERVICES IN A TERTIARY CARE HOSPITAL (RAJSHAHI MEDICAL COLLEGE) IN BANGLADESH

Monira Parveen*	Assistant Professor, Department of Pathology, Rajshahi Medical College, Rajshahi. *Corresponding Author
SM Asafudullah	Professor and Head, Department of Pathology, Rajshahi Medical College.
M. Rokeya Khatun	Associate Professor and Head , Department of Obstetrics and Gynecology, Rajshahi Medical College.
Md. Nowshad Ali	Professor, and Head, Department of Pediatric Surgery, Rajshahi Medical College.
Khadiza Khanom	Associate Professor, Department of Pathology, Rajshahi Medical college.
Arefa Sultana	Associate Professor, Department of Pathology, Rajshahi Medical college.

ABSTRACT Introduction: Colposcopy is done to detect cervical cancer and changes that may lead to cervical cancer. We aimed our study to observe the incidence of different pathologies of the cervix in Colposcopic specimens in Rajshahi Medical College of Bangladesh.

Materials and Methods: Retrospective data were collected from the routine histopathological laboratory in the department of pathology Rajshahi Medical College and were recorded during a study period of 1 year (July 2019 to June 2020).

Observations: Colposcopic biopsy is one of the commonest diagnostic procedures for assessing cervical Pathosis. Out of 641 specimens more than half, 365 specimens (56.50%) were Chronic Cervicitis. In present study, Chronic Cervicitis with squamous metaplasia and Invasive squamous cell carcinoma became the 2nd, 16.39% (105 specimens), and 3rd, 13.42% (86 specimens) most pathology involving the cervix. Cervical polyp, Endocervical and Leiomyomatous constitute 6.39% and 1.57% of the specimens respectively. 4.36% (28 specimens) of the study sample were the Intraepithelial neoplasia (CIN I, CIN III). Adenocarcinoma and Clear cell carcinoma constitute 0.79% and 0.16% of the study specimens. 50% of the cervical squamous cell carcinoma was moderately differentiated and well-differentiated and poorly differentiated squamous cell carcinoma constitutes 30.23% and 19.77% respectively.

Conclusions: Colposcopic examination of cervical biopsy specimens helps to detect the exact causes and underlined pathology.

## KEYWORDS: Colposcopic biopsy, Carcinoma, metaplasia, and CIN

### INTRODUCTION

Cervical cancer ranks third in cancer incidence worldwide and is the most frequent gynecological cancer in developing countries (Moshkovich et al., 2015; Benard et al., 2014, pp. 1004-1009). The frequency of cervical cancer after treatment for dysplasia is lower than 1% and mortality is less than 0.5% (Soutter et al., 1997, pp. 978-980). The increasing trend of the disease in developing countries is attributed to the early beginning of sexual activities, certain sexual behaviors like the high number of multiple partners, early age at first intercourse, infrequent use of condoms, multiple pregnancies with Chlamydia association, and immunosuppression with HIV, which is related to higher risk of HPV infection (Gustafsson et al., 1997, pp. 159-165). Histopathology forms the scientific and clinical basis for current prevention and treatment of cervical cancer. Histopathology determines the treatment of cancer and precancer through classifying into a diagnosis the patterns of microscopic organization of cells in tissue sections from the biopsy or surgical specimens. Although morphological concepts of cervical cancer and precancer evolution are giving way to viral and molecular knowledge, histopathology also remains important as the most widely used clinical endpoints by which the performance of new techniques for cervical cancer prevention are currently evaluated. Colposcopy is a medical diagnostic procedure to examine an illuminated, magnified view of the cervix as well as the vagina and vulva (Chase et al., 2009, pp. 472-480). Many pre-malignant lesions and malignant lesions in these areas have discernible characteristics that can be detected through the examination. It is done using a colposcopy, which provides a magnified view of the areas, allowing the colposcopist to visually distinguish normal from abnormal appearing tissue and take directed biopsies for further

pathological examination. The main goal of colposcopy is to prevent cervical cancer by detecting and treating precancerous lesions early. The procedure was developed by the German physician Hans Hinselmann (Halioua, 2010) with help from Eduard Wirths (Baggish & Michael, 2018). Most women undergo a colposcopic examination to further investigate a cytological abnormality on their Pap smears. Other indications for a patient to have a colposcopy include: i) assessment of diethylstilbestrol (DES) exposure in utero, ii) immunosuppression such as HIV infection, or an organ transplant patient, iii) an abnormal appearance of the cervix as noted by a primary care provider and iv) as a part of a sexual assault forensic examination (Archived copy, 2009). Colposcopy is not generally performed for persons treated for cervical cancer if their pap tests show a low-grade squamous intraepithelial lesion or less. Unless the person has a visible lesion, colposcopy for this population does not detect a recurrence of cancer (Rimel et al., 2011, pp. 548-553; Ergas et al., 2013, pp. 421-425)

#### **MATERIAL METHODS:**

This retrospective study was conducted in the Department of Pathology, Rajshahi Medical College, and Rajshahi for one year from July 2019 to June 2020. All the Colposcopic biopsy specimens sent to the pathology department during this study period included in the study as the sample. Clinical data about age, site of specimens, and histological diagnosis were recorded retrospectively. All the specimens were fixed in 10% formalin and tissue sections were taken for processing and paraffin block preparation. The paraffin blocks were sectioned and stained by H & E stain. A microscopical examination was performed for histopathological diagnosis. Histopathological diagnoses were analyzed along with type,

frequency, and percentage of cervical pathology and also the histological grade of squamous cell carcinoma of the cervix along with frequency and percentage.

## RESULT AND OBSERVATION:

Of the 1768 histopathology sample, 641 (36.25%) exhibited Colposcopic cervical pathology specimens (Figure 1). Out of 641 patients, about 38% of the patients were in their 3rd to 4th decade and another 32% in the 4th to 5th decade of life. About one-seventh (13 %) of patients were < 30 years old and about 17% study population were >50 years old. The mean age of the patients was 39.3 years (range: 17 - 80 years) (Table I). More than half, 365 specimens (56.50%) were Chronic Cervicitis (Table II). In this study, Chronic Cervicitis with squamous metaplasia and Invasive squamous cell carcinoma became the 2nd, 16.39% (105 specimens), and 3rd, 13.42% (86 specimens) most pathology involving the cervix (Table II). Cervical polyp, Endocervical and Leiomyomatous constitute 6.39% and 1.57% of the specimen's respectively (Table II). 4.36% (28 specimens) of my study sample were the Intraepithelial neoplasia (CIN I, CIN II, CIN III) (Table II). Adenocarcinoma and Clear cell carcinoma constitute 0.79% and 0.16% of the study specimens (Table II). 50 % of the cervical squamous cell carcinoma was moderately differentiated and well-differentiated and poorly differentiated squamous cell carcinoma constitutes 30.23% and 19.77% respectively (Table III).

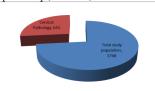


Figure 1: Distribution of study sample

Table I. Distribution of patients by demographic characteristics (n = 641)  $\,$ 

Demographic characteristics	Frequency	Percentage
Age		
< 30	82	12.79
30 – 39	246	38.37
40 – 49	206	32.14
50 – 59	61	7.18
≥ 60	46	9.52
Total	641	100%

Table II. Distribution of patients by Cervical pathology (n = 641)

Cervical pathology	Frequency	Percentage
Chronic Cervicitis	365	56.50
Chronic Cervicitis with squamous	105	16.39
metaplasia		
Invasive squamous cell carcinoma	86	13.42
Endocervical polyp	41	6.39
Leiomyomatous polyp	10	1.57
Intraepithelial neoplasia I (CIN I)	21	3.28
Intraepithelial neoplasia II (CIN II)	03	0.47
Intraepithelial neoplasia III	04	0.63
(CIN III)		
Adenocarcinoma	05	0.79
Clear cell carcinoma	01	0.16
Total	641	100%

Table III. Distribution of squamous cell carcinoma of cervix according to Histological grade (n=86)

Histological grading of Squamous	Frequency	Percentage
cell carcinoma		
Well differentiated	26	30.23
Moderately differentiated	43	50.00

Poorly differentiated	17	19.77
Total	86	100

#### DISCUSSION:

A colposcopy is a special way of looking at the cervix by using light and a low-powered microscope to make the cervix appear much larger. This helps the health care provider for finding and then taking biopsy from abnormal areas in cervix (Khan et al., 2017, pp. 223-229). The cervix and vagina are gently cleaned with a vinegar or iodine solution. This removes the mucus that covers the surface and highlights abnormal areas (Stoler et al., 2011, pp. 1354-1362). The provider will place the colposcope at the opening of the vagina and examine the area. Photographs may be taken. If any areas look abnormal, a small sample of the tissue will be removed using small biopsy tools (Benard et al., 2014, pp. 1004-1009). Sometimes a tissue sample from inside the cervix is removed (Newkirk, 2020).

Colposcopy is done to detect cervical cancer and changes that may lead to cervical cancer, an abnormal Pap smear or HPV test, bleeding after sexual intercourse, and also be done if the abnormality is seen in the cervix during a pelvic exam (Wheeler et al., 2013, pp. 198–207). These may include: i) Any abnormal growth on the cervix, or elsewhere in the vagina, ii) Genital warts or HPV, iii) Irritation or inflammation of the cervix (cervicitis), and iv) The colposcopy may be used to keep track of HPV, and to look for abnormal changes that can come back after treatment (Darragh et al., 2012, pp.1266–1297).

Cervical cancer starts in the cells on the surface of the cervix. the lower portion of the uterus. There are two types of cells on the surface of the cervix, squamous and columnar. Most cervical cancers come from these squamous cells (Kinney et al., 2014, pp. 628–635.). Cancer usually starts very slowly as a condition called dysplasia (Massad et al., 2013, pp. S1-S27; Castle et al., 2007, pp. 805–815). This precancerous condition can be detected by Pap smear and is 100% treatable. Undetected, precancerous changes can develop into cervical cancer and spread to the bladder, intestines, lungs, and liver. It can take years for these precancerous changes to turn into cervical cancer. However, patients with cervical cancer do not usually have problems until the cancer is advanced and has spread. Most of the time, early cervical cancer has no symptoms. Symptoms of advanced cancer may include back pain, bone fractures, fatigue, heavy vaginal bleeding, urine leakage, leg pain, loss of appetite, and pelvic pain. If after having a Pap smear, the doctor finds abnormal changes on the cervix, a colposcopy can be ordered.

Normal results, a smooth, pink surface of the cervix is normal (Stoler & Schiffman, 2001, pp. 1500–1505; Jordan et al., 2008, pp. 342-354). Abnormal results mean anything abnormality seen during the test, including abnormal patterns in the blood vessels, areas that are swollen, worn away, or wasted away (atrophic), cervical polyps, genital warts, whitish patches on the cervix, abnormal biopsy results may be due to changes that can lead to cervical cancer (Stoler et al., 2014, pp. 172-198; Salcedo et al., 2017). These changes are called dysplasia, or cervical intraepithelial neoplasia (CIN) (Spracklen et al., 2013, pp. 960–965.). CIN I is mild dysplasia, CIN II is moderate dysplasia, CIN III is severe dysplasia or very early cervical cancer called carcinoma in situ (Cohn et al., 2019; Smith, 2018). Abnormal biopsy results may be due to: Cervical cancer, Cervical intraepithelial neoplasia (precancerous tissue changes that are also called cervical dysplasia), and Cervical warts (infection with human papillomavirus, or HPV) (Dijkstra et al., 2010, pp. 972–977). If the biopsy does not determine the cause of abnormal results, then needs for a procedure called a cold knife cone biopsy.

According to the latest guidelines of the American Cancer Society, screening should begin at the age of 21 (Koss, 1992, pp. 314-370). Younger women should be screened neither with

Pap test nor with the HPV test. Women between 21-29 years should be screened with a Pap test every 3 years. In women between 21-29 years, who have had two or more consecutive negative cytology results, data are not adequate to assert a larger interval time between screening (>3 years). The HPV test should be used in these ages only after Pap test abnormal findings. Women between 30-65 years should be screened with both Pap test and HPV test (co-testing) every 5 years. This type of screening is preferable, but continuing Pap test screening every 3 years is also acceptable. Data is inadequate to support longer interval time between tests in this age group after several negative tests (Saslow et al., 2012, pp. 516-542).

The most common histopathological diagnosis of the present study among 641 cervical lesions was Chronic cervicitis comprised of 365 cases (56.50%) which is similar to the study conducted by Saravanan et al. (2015) 58.6% and Pandit et al. (2016) 61.83%. In the present study cervical cancer accounted for 12.94% cases of all cervical lesions which was comparable to the study done by Saravanan et al. (2015) and Sinha et al (2011) whereas it was less when compared to Jyothi et al. (2015). In the present study squamous cell carcinoma was the commonest of the invasive lesions encountered in this study, accounting for 93.47% of the total invasive carcinoma which was comparable with the study of Shruthi et al. (2014) and Oguntayo et al. (2011). This study reported 43 cases (50%) out of 86 cases of squamous cell carcinoma as moderately differentiated. This finding was in accordance with the study of Shruthi et al. (2014) who also found majority (55.90%) of cases of squamous cell carcinoma of moderately differentiated type.

#### **CONCLUSION:**

As the precancerous conditions can be detected by Colposcopic biopsy and is 100% treatable in addition to diagnose other pathologies involving cervix, Colposcopic examination should be included as a preventive routine diagnostic examination of vagina and cervix with Pap smear and HPV DNA test.

## REFERENCES:

- "Ārchived copy". Ārchived from the original on 2009-12-22. Retrieved 2010-02-
- Baggish, & Michael, S. (2018 April). Colposcopy of the Cervix, Vagina, and Vulva-A Comprehensive Textbook. Mosby. ISBN 9780323018593. Retrieved 11 April 2018 – via Google Books.
- Benard, V.B., Thomas, C.C., King, J., Massetti, G.M., Doria-Rose, V.P., & Saraiya, M.(2014). Vital signs: cervical cancer incidence, mortality, and screening – the United States, 2007-2012. Morbidity and Mortality Weekly Report, 63(44), 1004-1009.
- Castle, P.E., Stoler, M.H., & Solomon, D. (2007). The relationship of community biopsy-diagnosed cervical intraepithelial neoplasia grade 2 to the quality control pathology-reviewed diagnoses: an ALTS report. American journal of clinical Pathology, 127, 805–815.
- Chase, D.M., Kalouyan, M., & Di Saia, P.J. (2009 May). Colposcopy to evaluate abnormal cervical cytology in 2008. American Journal of Obstetic and Gynecology. 200 (5), 472–480. Available from: doi:10.1016/j.ajog.2008.12.025. PMID 19375565.
- Cohn, D.E., Ramaswamy, B., Christian, B., & Bixel, K. (2019). Malignancy and pregnancy. In: Resnik, R., Lockwood, C.J., Moore, T.R., Greene, M.F., Copel, J.A., Silver, R.M (Eds.) Creasy and Resnik's Maternal-Fetal Medicine: Principles and Practice. 8th ed., chap 56). Philadelphia, PA: Elsevier.
- Darragh, T.M., Colgan, T.J., & Cox, J.T. (2012). The lower anogenital squamous terminology standardization project for HPV-associated lesions: background and consensus recommendations from the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology. Archives of Pathology & Laboratory Medicine, 136, 1266–1297
- Dijkstra, M.G., Heideman, D.A., & De Roy, S.C. (2010). Immunostaining as an alternative to histology review for reliable grading of cervical intraepithelial lesions. Journal of Clinical Pathology, 63, 972–977.
- Ergas, A.I., Havrilesky, L.J., Fader, A.N., Guntupalli, S.R., Huh, W.K., Massad, L.S., & Rimel, B.J. (2013). "Cost analysis of colposcopy for abnormal cytology in post-treatment surveillance for cervical cancer". Gynecologic Oncology, 130 (3), 421-425. Available from: doi:10.1016/j.ygyno.2013.05.037. PMID 23747836
- Gustafsson, L., Pontén, J., Bergström, R., & Adami, H.O.(1997). International incidence rates of inva-sive cervical cancer before cytological screening. *International Journal Cancer*, 71,159-165.
- Halioua, B. (2010). The Participation of Hans Hinselman in Medical Experiments at Auschwitz. Journal of Lower Genital Tract Disease, 14 (1): 1–4.
   Available: from doi:10.1097/LGT.0b013e3181af30ef. PMID 20040829.

- Jordan, J., Arbyn, M., Martin-Hirsch, P., Schenck, U., Baldauf, J-J., Da Silva, D., Anttila, A., Nieminen, P., & Prendiville, W. (2008). European guidelines for quality assurance in cervical cancer screening: recommendations for clinical management of abnormal cervical cytology, part 1. Cytopathology, 19 (6), 342–354. Available from: doi:10.1111/j.1365-2303.2008.00623.x. ISSN 0956-5507. PMID 19040546
- Jyothi, V., Manoja, V., & Sridhar, K. (2015). A clinicopathological study on cervix. J Evol Med Dent Sci. 4(13), 2120–2126.
- Khan, M.J., Werner, C.L., & Darragh, T.M.(2017). ASCCP colposcopy standards: role of colposcopy, benefits, potential harms and terminology for colposcopic practice. *Journal of Lower Genital Tract Disease*. 21(4), 223-229. PMID: 28953110 pubmed.ncbi.nlm.nih.gov/28953110/.
- Kinney, W., Hunt, W.C., & Dinkelspiel, H. (2014). Cervical excisional treatment of young women: a population-based study. Gynecology Oncology, 132, 628–635.
- Koss, L.G.(1992). Chapter Part I: Inflammatory processes; Part II: Other benign disorders of the cervix and vagina. In: R. Winters, E. Orem & T. Gibbons (Eds). Diagnostic Cytology (4th ed., pp 314-370). Philadelphia: JB Lippincott Co.
- Massad, L.S., Einstein, M.H., & Huh, W.K. (2013). 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *Journal of Lower Genital Tract Diseases*, 17, S1–S27.
- Moshkovich, O., Lebrun-Harris, L., & Makaroff, L. (2015). Challenges and opportunities to improve cervical cancer screening rates in US Heath center through patient-centered medical home transformation. Advanced Preventive Medicine, 2015, 182073. https://doi.org/10.1155/2015/182073.
- Newkirk, G.R. (2020). Colposcopic examination. In: Fowler, G.C. (Eds). Pfenninger and Fowler's Procedures for Primary Care. (4th ed., chap 124.). Philadelphia, PA: Elsevier.
- Oguntayo, O.A., Zayyan, M., Kolawole, A.O., Adewuyi, S.A., Ismail, H.& Koledade, K. (2011). Cancer of the cervix in Zaria. Northern Nigeria E-cancer medical science, 5, 219.
- Pandit, G.A., Khiste, J.A., & Jindal, S.( 2016). Study of histomorhological spectrum of lesions of uterine cervix. *Int J current research*, 8(05), 30724-30727.
   Rimel, B.J., Ferda, A., Erwin, J., Dewdney, S.B., Seamon, L., Gao, F., Desimone,
- Rumel, B.J., Ferad, A., Erwin, J., Dewaney, S.B., Seamon, L., Gao, F., Desimone, C., Cotney, K.K., Huh, W., & Massad, L.S. (2011). Cervicovaginal Cytology in the Detection of Recurrence After Cervical Cancer Treatment. Obstetrics & Gynecology, 118(3): 548–553. Available from: doi:10.1097/AOG.0b 013e 3182 27164d PMID:121860282
- Salcedo, M.P., Baker, E.S., & Schmeler, K.M. (2017). Intraepithelial neoplasia
  of the lower genital tract (cervix, vagina, vulva): etiology, screening,
  diagnosis, management. In: Lobo, R.A., Gershenson, D.M., Lentz, G.M.,
  Valea, F.A. (Eds.) Comprehensive Gynecology (7th ed., chap 28.).
  Philadelphia, PA: Elsevier.
- Saslow, D., Solomon, D., & Lawson, H.W. (2012). American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. American Journal of Clinical Pathology, 137, 516-542.
- Saravanan, S., Arnold, J., & Arul, P. (2015). Histomorphological Spectrum of lesions of the cervix, a Retrospective Study in a Tertiary Care Hospital. J Evol Med Dent Sci. 4(59), 10326–10329.
- Sinha, P., Rekha, P.R., Subramaniam, P.M., Konapur, P.G., Thamilselvi, R.& Jyothi, B.L. (2011). A clinicomorphological study of carcinoma cervix. National Journal Of Basic Medical Sciences, 2(1), 4–7
- Shruthi, P.S., Kalyani, R. & Kai, L.J.(2014). Narayanaswamy. Clinicopathological correlation of cervical carcinoma: A tertiary hospital based study. Asian Pac J Cancer Prev, 15(4), 1671-1674.
- Smith, R.P.(2018). Carcinoma in situ (cervix). In: Smith, R.P.(Eds). Netter's Obstetrics & Gynecology (3rd ed., chap 115.). Philadelphia: PA: Elsevier.
- Spracklen, C. N., Harland, K. K., Stegmann, B. J., & Saftlas, A. F. (2013). Cervical surgery for cervical intraepithelial neoplasia and prolonged time to conception of live birth: A case-control study ". BJOG: An International Journal of Obstetrics & Gynaecology, 120(8), 960–965. Available from: doi:10.1111/ 1471-0528.12209. PMC 3691952. PMID 23489374
- Soutter, W.P., de Barros Lopes, A., & Fletcher, A. (1997). Invasive cervical cancer after conservative therapy for cervical intraepithelial neoplasia. *Lancet* 349, 978-980.
- Stoler, M.H., Vichnin, M.D., & Ferenczy, A. (2011). The accuracy of colposcopic biopsy: analyses from the placebo arm of the Gardasil clinical trials. International Journal of Cancer, 128, 1354–1362.
- Stoler, M.H., & Schiffman, M. (2001). Interobserver reproducibility of cervical cytologic and histologic interpretations: realistic estimates from the ASCUS-LSIL Triage Study. *Journal of the American Medical Association*, 285, 1500–1505.
- Stoler, M., Bergeron, C., & Colgan, T.J. (2014). Epithelial tumors, part of tumors of the uterine cervix, chapter 7. In: Kurman, R.J., Carcangiu, M.L., Herrington, C.S., Young, R.H. (Eds.). WHO Classification of Tumours of Female Reproductive Organs (4thed. pp 172-198). Lyon: IARC.
- Wheeler, C.M., Hunt, W.C., & Cuzick, J.(2013). New Mexico HPV Pap Registry Steering Committee. A population-based study of human papillomavirus genotype prevalence in the United States: baseline measures prior to mass human papillomavirus vaccination. International Journal of Cancer, 132.198–207