

A Comprehensive Study of Cervical Carcinoma based on Manual Screening Techniques

R. Rajpriya*¹ and Dr.M.S.Saravanan*²

¹ Research scholar, Department of Computer Science,
Bharathiar University, Coimbatore,
India.

² Department of Computer Science and Engineering,
Savitha University, Chennai,
India.

Abstract

Cervical cancer is the second most common cancer among worldwide affected by women. Indian council of medical research estimated one lakh new cases are affected with cervical cancer in the year of 2016. ICMR expected 30 percent of tobacco users are affected by cervical cancer. It is caused by the virus is called Human Papilloma Virus (HPV). The conventional method of diagnosing the cervical cancer is Pap smear test. Pap test is used to reduce the incidence and mortality rate of cervical cancer. We need to concentrate in objective, specific and cost-effective screening of cervical cancer for getting better results. Cervical cancer is usually affected in the age group 35-55 years of women. The aim of study is to establish the accurate and quick diagnostic methods and the methods are used to differentiate the benign and malignant tissues. Colposcopy is used to examine the parts of vagina, vulva and the cervix and it is easily identifying the abnormal cells. Manual techniques are leads to produce high false-positive rate due to human error and it suffers from accurate results and time consuming. Automated techniques are achieved accurate results based on cytology data and electromagnetic spectra data.

Keywords: Cervical cancer, Pap smear, Human Papilloma Virus(HPV), Colposcopy.

1. Introduction

Cervix is the lower and narrow part of the uterus(womb). It is in abdomen, between the bladder and rectum. Its length is 2-3cm and its shape is cylinder²⁻³. The lower part of the cervix is ectocervix. A cervical canal connects the body of the uterus(Fig.1). Cervical canal lining with mucosa called endocervix and covering the ectocervix with mucosa called exocervix. The shape of the ectocervix is convex and elliptical shapes and its long is 3cm and wide is 2.5cm. The endocervical

mucosa lined with a single layer of columnar cells and the ectocervical covered with squamous epithelia and the junction between these two types of epithelial is called squamocolumnar junction.

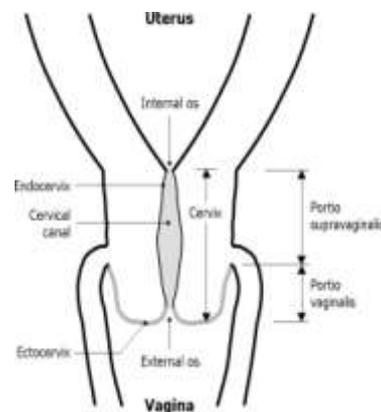


Fig.1 Image of Uterus and Cervix

Cancer begins with the surface of the cervix, the healthy cells are growing out of control and forming a mass called a tumor. There are two types of tumors, benign and malignant. The benign tumor has not spread, and the malignant tumor has spread to other parts of the body. The outer lining cells of the cervix (squamous cells) affected by cancer called squamous cell carcinoma which arises from 80% to 90%. The inner lining cells of the cervix (glandular cells) affected by cancer called adenocarcinoma which arises from 10% to 20%. Abnormal changes of the cells in the cervix called dysplasia which indicates precancerous cervical cells. Pap test is used to identifying the dysplasia is referred to as a Squamous Intraepithelial Lesion (SIL)⁴⁻⁵.

Human Papilloma Virus (HPV) is the sexually transmitted disease and it is transmitted through skin-to-skin contact. HPV affected the human and it caused by various health problems such as genital warts and cancer (Fig.2). Cervical cancer associated with two types of HPV, such as HPV16 and HPV18 which affected by around 70% cases. Nearly, there are 170 types of HPV's are differentiated and more than 40 types of HPV's are transmitted through sexual contact. Some HPV types are 16,18,31,33,35,39,45,51,52,56,58,59 and 68 are associated with carcinogenic. HPV infection indicates differences and immature of squamous epithelium and disrupted of E6/E7 oncoproteins and normal growth are affected by these types of HPV⁶⁻⁷. These infections are involved the basement membrane becomes invasive cancer and affected with the surrounding of tissues and organs. These infections are spread throughout the lymph nodes and distant organs.



Fig.2 Human Papilloma Virus

Cervical Intraepithelial Neoplasia (CIN) occurs on the cervix at the place of Squamous Intraepithelial Lesion (SIL). Pap test has used to identify the CIN which classify the changes of precancerous in the cervix and the final decision are taken by histopathology examination. After test, CIN has categorized into thickness of the epithelium and it concerned with immature, differentiated cells with nuclear abnormalities. The proportion of the thickness of epithelium is used to grade the CIN

degrees. CIN is categorized into three grades, CIN1, CIN2, CIN3. The grade CIN1 is affected by minimum abnormalities are present in the nucleus and few mitotic figures are seen. CIN1 represents mild dysplasia, and it is confined by 1/3 of the epithelium. CIN2 represents moderate dysplasia, mix of low and high-grade lesions, and it is confined by 2/3 of the epithelium. CIN2 is characterized by nuclear abnormalities and mitotic figures are seen throughout the epithelium. CIN3 represents severe dysplasia and it is confined by 2/3 of the epithelium. In CIN3, many abnormalities of nucleus are present throughout the epithelium and several abnormal forms of mitotic figures are present in the epithelium⁸⁻⁹.

Staging of cancer is used to identifying where the cancer has located or where it has starts and spread and whether it has affected by other parts of the body. There are four stages, such as stage I, II, III and IV. In stage I, cancer has found in the uterus and the cancer has affected in the lining of the cervix and it has not spread to other parts of the body. In this stage, there are several stages are used to identify the cancer, such as stage IA, IA1, IA2 and IB, IB1, IB2 are diagnosed by microscopy and these stages of cancer has affected with smaller length¹⁰⁻¹¹. It has not involved in lymph nodes and has not spread to distant organs. In stage II, cancer spread to nearby areas are surrounding by cervix. But it has not spread to other organs (Fig.3). In this stage, the other stages are involved in this process, such as stage IIA, IIA1, IIA2 and IIB are not involved to lymph nodes and other parts of the body. In stage III, cancer has affected the part of vagina and the cancer has spread to pelvic wall and it causes kidney swelling and kidney failure. The other stages are IIIA and IIIB are not involved to lymph nodes and other organs. In stage IV has involved two stages, such as IVA and IVB. In stage IVA, cancer has spread to bladder and rectum and may or may not have spread to other organs. In stage IVB, cancer has spread to other parts of the body.

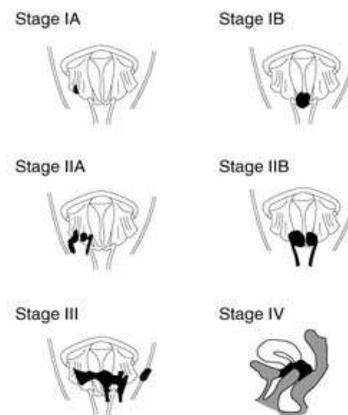


Fig.3 Stages of cancer

In the early stage, the symptoms are vaginal discharge, irregular bleeding, postcoital spotting, postmenopausal spotting, etc. In the advanced stage, urinary frequency, backache, lower abdominal pain, severe back pain, weight loss, renal failure, swelling of the lower limbs, and breathlessness¹²⁻¹³. Risk factor means a person increases the chances of developing cancer. The factors are Human Papilloma Virus (HPV) infection, immune system deficiency, herpes, smoking, ethnicity, oral contraceptives, exposure to diethylstilbestrol (DES)¹⁴⁻¹⁵.

2. Materials and methods

Early detection can prevent the cervical cancer and the cancer screening is achieved in the age group of women is around 30-40 years. The treatment is based on screening test and it can reduce the time lag for receive treatment. Screening is used to identify the disease itself or a precursor of the disease. To diagnose the stage of cancer, first we learn if cancer has spread to other parts of the body. Several tests are useful for diagnosing the cancer and staging the grade of the cancer¹⁶.

2.1. Pelvic Examination:

To examine the abnormal changes are present in the parts of uterus, vagina, ovaries, cervix, bladder and rectum.

2.2. Cytology (Pap Test):

Pap test is used to taking a sample of cells from the cervix at the place of transformation zone. After taking the samples, the cells are placed in the slide or transport medium and sent to the laboratory for examining the cells under the microscope¹⁸⁻¹⁹. Cytology requires the speculum and light source for visualizing the surface of the cervix. The samples are taken from the cervix using with spatula or brush and transfer the samples in a container with some preservative solution and sent to the laboratory for further examination. Pap test is referred to Thin prep test, the samples are removed from the mucus and blood and the samples are transfer a thin layer of cells into the slide and the test can be done by histopathology examination (Fig.4). Computers are used to scan the abnormal cells are present in the sample are called Auto pap or Focal Point method.

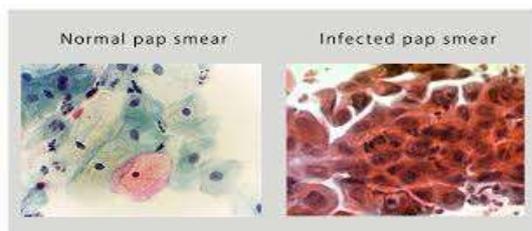


Fig.4 Pap Smear Images

2.3. HPV Testing:

This test is based on detection of DNA from high-risk HPV types in the samples. If the infection is persistent means the high-risk HPV type is detected. This test is used to reduce the risk of future cervical cancer and does not require the examination of pelvic and cervix. For collecting the sample of cells, inserting a small brush or any other device into the vagina and scrape the tissues from the cervix and place it in the container with preservative solution and it has sent to the laboratory for speculum examination.

2.4. Visual Screening Methods:

Visual inspection with acetic acid (VIA) is used to detecting the abnormal changes of the cells. VIA is used with speculum and applying dilute (3-5%) acetic acid in the surface of the cervix⁹. After diluting, it can easily inspect the cervix and easily visible the squamocolumnar junction. VIA requires speculum, light source and acetic acid(3-5%). It is used to identify the squamocolumnar junction and inspect the cervix has affected with precancer or cancer. After applying the acetic acid in the surface of the cervix with a cotton swab. After one minute, the infected areas are become faintly white due to the changes of cells(metaplasia). After one minute, the acetowhite changes are not present in the cervix which is associated precancer or cancer. If these changes are noted which is considered as a positive result and there are no changes are noted, it become a negative report. VIA testing is used to detect the early stage of cancer or advanced level of cancer.

2.5. Colposcopy:

It is used to examine the epithelial layers and surrounding blood vessels which provides the visualization of the parts, such as cervix, vulva and vagina. Colposcope is an instrument with strong light is used to magnifies the cells are present in the cervix.

2.6. Biopsy:

It is used to determine the degree of abnormalities of the cell changes. This method is used to classify the cells are normal or as invasive cancer and it is classified the precancerous lesions as low-grade(CIN1) or high-grade (CIN2 and CIN3). The degree of CIN is based on the thickness of the epithelium and the abnormal changes are present in the basement membrane. CIN1 has affected with mild abnormality and low-risk HPV type and so CIN1 is not treated to cancer. CIN2+ are high-risk HPV type which is affected moderate or severe cancer and it is referred to treated²⁰⁻²¹.

2.7. Endocervical curettage:

ECC is a procedure, to scrape the surface cells from the cervical canal using with spatula or an instrument and the tissue is placed in the container with preservative solution and the samples are sent to the laboratory for further examination. ECC is used with small, spoon-shaped instrument to scrape the tissue from the cervix.

2.8. X-ray:

It is used to view the structure of pictures to from inside the body used with some radiations.

2.9. Computed tomography:

It visualizes the picture in 3-dimensional view and it shows the abnormalities of cells are present in the cervix. This method is used with a special dye for providing better images and to measuring the size of tumors.

2.10. Magnetic Resonance Imaging (MRI):

It produces the size of the tumors and it provides the details of the image of the cervix. The special dye is used to give the better images and the dye is given to the patients before the scanning process²²⁻²³.

2.11. Positron Emission Tomography (PET) or PET-CT scan:

This method is used to combined with CT scan called PET-CT scan. PET scan is used to picturize the organs and tissues of the body. The small amount of radioactive sugar is injected into the body because of the affected cancer cells are absorb more energy to collecting the samples. This sugar substance is used to produce the images of affected areas are present from inside of the body²⁴⁻²⁵.

2.12. Cystoscopy:

It is a procedure used to view the images of bladder and urethra. Cystoscopy used with thin, lighted tube for viewing the parts of the body. An instrument is used for imaging process called cystoscope²⁶⁻²⁷. This method is used to determine the cancer cells whether the cancer has spread to the bladder or other parts of the body.

2.13. Proctoscopy:

This procedure is used to view the images of colon and rectum. An instrument used with thin, lighted and flexible tube is inserted into the rectum called sigmoidoscope²⁸. This method is used to determine and view the cancerous cell which has spread to the rectum, colon, and distant organs.

2.14. Laparoscopy:

It is a procedure is used to view the abdominal images. An instrument used with thin, lighted and flexible tube is inserted through an incision in the body called laparoscope.

3. Results and Discussion:

If the screening test revealed as a high-grade lesion, the patient referred for Loop Electrosurgical Excision Procedure (LEEP) or Cold Knife Conization (CKC). After the examination, the cervix is identified as a pre-cancer, the treatment methods may be ablative (destroying the abnormal tissues) or excision (removing the abnormal tissues). The treatment methods are Cryotherapy, Loop Electrosurgical Excision Procedure (LEEP) and Cold Knife Conization (CKC)²⁹⁻³⁰.

3.1. Cryotherapy:

It eliminates the abnormal cells are affected on the cervix by freezing. To applying a high cooled metal disc (cryoprobe) to the cervix and freezing the area affected by the cancer. The cryoprobe is compressed with carbon dioxide (CO₂) or nitrous oxide (NO₂) gas is accomplished in the tank.

3.2. Loop Electrosurgical Excision Procedure (LEEP):

This method is used to remove the abnormal areas from the cervix using a loop with thin wire powered by an electrosurgical unit. The loop is used to cut and coagulate the area using with ball electrode. LEEP is used to remove the affected lesions and the tissues are sent to the histopathology examination.

3.3 Cold Knife Conization (CKC):

This method is used to remove the cone-shaped area from the cervix, including inner and outer portions of the cervix. The abnormal tissues are completely removed and sent to the pathology examination. The procedure tasks around one hour and it is performed under anesthesia.

4. Conclusion:

Cervical cancer is diagnosed by pap smear, liquid-based cytology, colposcopy and other various tests which does not give accurate results of detecting normal and abnormal cells in the region of the cervix. The manual screening process suffers from high false-positive rate and low false-negative rate due to human error and it is very cost effective for diagnosing by experts. The computer-aided techniques are performed to produce better results of

detecting and classifying the cancerous cells. In future, various techniques will be used detecting, extracting and classifying the cancerous cells are present in the region of the cervix.

References

- [1] WHO/ICO Information Centre on HPV and Cervical cancer summary report on HPV and Cervical cancer statistics in India 2017.
- [2] World Health Organization, 2014, Comprehensive cervical cancer: a guide to essential practice.
- [3] ICMR, Over 17 lakh new cancer cases in India by 2020.
- [4] H. S. Cronjé, "Screening for cervical cancer in the developing world," *Best Practice and Research: Clinical Obstetrics and Gynaecology*, vol. 19, no. 4, pp. 517–529, 2005.
- [5] J. T. Bryan, F. Taddeo, D. Skulsky et al., "Detection of specific human papillomavirus types in paraffin-embedded sections of cervical carcinomas," *Journal of Medical Virology*, vol. 78, no. 1, pp. 117–124, 2006.
- [6] E. M. Kanter, E. Vargis, S. Majumder et al., "Application of raman spectroscopy for cervical dysplasia diagnosis," *Journal of Biophotonics*, vol. 2, no. 1-2, pp. 81–90, 2009.
- [7] C. M. Krishna, N. B. Prathima, R. Malini et al., "Raman spectroscopy studies for diagnosis of cancers in human uterine cervix," *Vibrational Spectroscopy*, vol. 41, no. 1, pp. 136–141, 2006.
- [8] Reading a Pathology Report, Approved by the Cancer.Net Editorial Board, 01/2016
- [9] M. F. Parker, J. P. Karins, and D. M. O'Connor, "Hyperspectral diagnostic imaging of the cervix: initial observations," in *Proceedings of the IEEE Pacific Medical Technology Symposium*, pp. 144–148, Honolulu, Hawaii, USA, August 1998.
- [10] S. J. Keenan, J. Diamond, W. Glenn McCluggage et al., "An automated machine vision system for the histological grading of cervical intraepithelial neoplasia (CIN)," *Journal of Pathology*, vol. 192, no. 3, pp. 351–362, 2000.
- [11] R. A. Kerkar and Y. V. Kulkarni, "Screening for cervical cancer: an overview," *Obstetrics and Gynecology of India*, vol. 56, no. 2, pp. 115–122, 2006.
- [12] M. F. K. Fung, M. Senterman, P. Eid, W. Fought, N. Z. Mikhael, and P. T. T. Wong, "Comparison of fourier-transform infrared spectroscopic screening of exfoliated cervical cells with standard papanicolaou screening," *Gynecologic Oncology*, vol. 66, no. 1, pp. 10–15, 1997.
- [13] L. Chiriboga, P. Xie, H. Yee, D. Zarou, D. Zakim, and M. Diem, "Infrared spectroscopy of human tissue. IV. Detection of dysplastic and neoplastic changes of human cervical tissue via infrared microscopy," *Cellular and Molecular Biology*, vol. 44, no. 1, pp. 219–229, 1998.
- [14] R. Sindhuphak, S. Issaravanich, V. Udomprasertgul et al., "A new approach for the detection of cervical cancer in Thai women," *Gynecologic Oncology*, vol. 90, no. 1, pp. 10–14, 2003.
- [15] S. G. El-Tawil, R. Adnan, Z. N. Muhamed, and N. H. Othman, "Comparative study between Pap smear cytology and FTIR spectroscopy: a new tool for screening for cervical cancer," *Pathology*, vol. 40, no. 6, pp. 600–603, 2008.
- [16] M. F. Parker, J. P. Karins, and D. M. O'Connor, "Hyperspectral diagnostic imaging of the cervix: initial observations," in *Proceedings of the IEEE Pacific Medical Technology Symposium*, pp. 144–148, Honolulu, Hawaii, USA, August 1998.
- [17] C. Balas, "A novel optical imaging method for the early detection, quantitative grading, and mapping of cancerous and precancerous lesions of cervix," *IEEE Transactions on Biomedical Engineering*, vol. 48, no. 1, pp. 96–104, 2001.
- [18] A. Stafil, "Cervicography: a new method for cervical cancer detection," *The American Journal of Obstetrics and Gynecology*, vol. 139, no. 7, pp. 815–825, 1981.
- [19] D. V. Coleman, "Evaluation of automated systems for the primary screening of cervical smears," *Current Diagnostic Pathology*, vol. 5, no. 2, pp. 57–64, 1998.
- [20] K. Losell and A. Dejmek, "Comparison of papnet-assisted and manual screening of cervical smears," *Diagnostic Cytopathology*, vol. 21, no. 4, pp. 296–299, 1999.
- [21] W. Li, J. Gu, D. Ferris, and A. Poirson, *Automated Image Analysis of Uterine Cervical Images*, STI Medical Systems, S.M. Systems, Honolulu, Hawaii, USA, 2007.
- [22] H. Greenspan, S. Gordon, G. Zimmerman et al., "Automatic detection of anatomical landmarks in uterine cervix images," *IEEE Transactions on Medical Imaging*, vol. 28, no. 3, pp. 454–468, 2009.

- [23] K. Krishnaveni, S. Allwin, S. P. K. Kenny, and G. Mariappan, "Analysis for textural features in nuclei of cervical cyto images," in Proceedings of the IEEE International Conference on Computational Intelligence and Computing Research (ICCIC '10), pp. 943–947, Coimbatore, India, December 2010.
- [24] R. F. Walker, P. Jackway, B. Lovell, and I. D. Longstaff, "Classification of cervical cell nuclei using morphological segmentation and textural feature extraction," in Proceedings of the 2nd Australian and New Zealand Conference on Intelligent Information Systems, pp. 297–301, December 1994.
- [25] S. Y. Park, M. Follen, A. Milbourne et al., "Automated image analysis of digital colposcopy for the detection of cervical neoplasia," *Journal of Biomedical Optics*, vol. 13, no. 1, Article ID 014029, 2008.
- [26] Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. GLOBOCAN 2012 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: <http://globocan.iarc.fr>.
- [27] Knowledge and awareness of cervical cancer among women in rural india, Arunadevi V.1, Geetha Prasad2, Vol 7 • Issue 21 • November 2015
- [28] Incidence and risk factors of most prevalent cancers in india, *Int J Pharm Bio Sci* 2015 April; 6(2): (B) 436 – 443, bakhyashree* and radhasaraswathy* *Vellore. Tamilnadu, India*
- [29] Vibrational Microspectroscopy for Cancer Screening, Fiona M. Lyng, Ines R. M. Ramos, Ola Ibrahim and Hugh J. Byrne *Appl. Sci.* 2015
- [30] Optical spectroscopy for detection of neoplasia, Konstantin Sokolov*, Michele Follen† and Rebecca Richards-Kortum, *Current Opinion in Chemical Biology* 2002, 6:651–65.