

Pap screening for cervical carcinoma – evolving trends

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Abstract

Cancer has manifested itself as one of the most serious health problems facing humanity today. Cervical cancer is one of the most common types of cancer, and the Papanicolaou (Pap) test, often known as a Pap smear, is the most basic test for cervical screening. It involves the microscopic inspection of cervical cells obtained from the cervix, and it is performed by a physician. In order to achieve this, automated detection and classification of cervical cancer from pap-smear images has become a must just because it allows for accurate, reliable, and rapid investigation of the condition's progression. With an emphasis on the history of pap screening, liquid based cytology, and machine learning for cervical cancer detection in recent research publications, this paper provides a summary of the state of the art as stated in several significant recent information sources. For the first time, an evaluation of image analysis and machine learning applications in the growing trends of cervical cancer diagnosis from pap-smear images over the course of a decade has been published. The survey examines 26 journal papers that were obtained electronically through major scientific databases such as PubMed, Google Scholar, Scopus, IEEE, and Science Direct, which were searched using sets of keywords. The papers were obtained from major scientific databases such as Pubmed, Google Scholar, Scopus, IEEE, and Science Direct. Whenever the Pap test is improved through the use of artificial intelligence, the sensitivity for the detection of cervical pathology is improved as well. The general public should be taught about the Pap smear test with AI, including its purpose and the frequency with which it must be performed, through comprehensive programmes aimed at improving disease management in general.

Key words - Pap smear, liquid based cytology, artificial intelligence, cervical cancer screening.

1.0 INTRODUCTION

Among the most common cancers worldwide, cervical cancer is the third most common, and it is the most common gynecological cancer in developing countries. Every year, it is estimated that 500,000 new cases are reported throughout the world, with the vast majority (80%) occurring in underdeveloped countries [1]. The disease is most typically discovered in people in their fifth decade of life, which is several years earlier than the median age at which breast, lung, and ovarian cancers are first discovered. Comparing cervical cancer to other cancers for which screening is regularly suggested, the likelihood that a particular woman would acquire invasive cervical cancer in the next year (incidence) is low when compared to other cancers [2].

Every year, over 73,000 women die in India as a result of the Cervical Cancer disease. India is the country with the highest number of cervical cancer deaths in the world, according to the

World Health Organization [3]. According to a report published by a research and advocacy organisation based in the United States. According to the World Health Organization, India accounts for 26.4 percent of all women who die from cervical cancer worldwide. China, Bangladesh, Pakistan, Indonesia, and Thailand also have significant death rates from cervical cancer [4].

Annual incidence rates begin to grow slowly around the age of 35 to 39 and shortly reach a plateau of approximately 20 per 100,000 people. The incidence of carcinoma in situ is higher than that of other cancers, peaking at approximately 130 per 100,000 in the age group 25 to 35 and subsequently dropping to approximately 20 per 100,000 by age 50. Cervical cancer is highly avoidable with the use of cytological screening programmes, which aid in the detection and treatment of precancerous lesions in the early stages of the disease. As a result of the need for a well-established laboratory, highly trained technicians, and up to three visits for screening, evaluation of cytological abnormalities, and treatment, such screening is difficult to implement and maintain in resource-constrained settings, and is therefore difficult to sustain in resource-constrained settings [5].

Instead of relying on existing laboratory infrastructure, alternative methods, such as DNA testing for human papillomavirus (HPV) and simple visual screening, may prove more practical when integrated into new strategies that require fewer visits and are less dependent on existing laboratory infrastructure. The significantly lower incidence of cervical cancer in industrialised countries has been attributed to screening programmes that have been implemented in these countries over the last 50 years, and cervical cancer screening has emerged as the gold standard for effective cancer prevention through the detection of preneoplastic lesions in the early stages of the disease [6]. In industrialised countries, considerable percentages of healthcare resources are spent on cancer screening in order to achieve low cancer incidence rates through adequate screening. The frequent retesting and tedious workup of inconclusive test findings that are required to ensure the safety of current screening programmes are extremely expensive. As a result, the majority of the money spent on this cancer prevention programme is due to the inherent limitations of the assays in identifying people who require further medical intervention after being diagnosed with cancer. In contrast to cases missed by screening, it is hypothesized that many cancer cases that continue to occur despite frequent screening programmes are attributable to failure to participate in screening rather than cases missed by screening itself [7].

The pathologist examines the slides under a microscope to see if any abnormal cells have spread throughout the slide. On the basis of the analysis, cancer is ruled out. The diagnosis made by pathologists can be inconsistent because of the subjectivity that governs slide interpretation, as well as the fact that the analysis of cancer is dependent on the skill and competency of the pathologist. When untrained pathologists do not have access to appropriate guidance, problems can develop [8]. It is therefore necessary to provide a system that can aid pathologists during the diagnostic process, thereby reducing the amount of subjectivity associated with diagnosis.

It is necessary to provide a precise and persistent automated by computer system for cervical cancer detection in order to assist in resolving the problem of persistent and examination skills of

lab staff as well as to reduce the level of subjectivity. The primary goal of the automatic cancer detection system is to assist practitioners in better comprehending medical images, consequently promoting the prevention of health check-ups for the purpose of preventing premature cancer diagnosis [9]. The evolution of imaging technology has resulted in a considerable improvement in the quality of medical images, which has resulted in more accurate diagnosis. The use of biopsy tests can therefore aid in the diagnosis and classification of disorders in medical analysis. The ideal situation would be for all cervical malignancies to be diagnosed as premalignant lesions and treated before they progress to invasive cervical cancer [10]. As a result, the diagnosis of an invasive cervical cancer signals a failure in the cancer screening process. So the current review article goes into great detail regarding the most recent developments in cervical cancer screening techniques.

2.0 DIAGNOSIS AND SCREENING TESTS FOLLOWED

In the developing world, only a few screening procedures have been proved to be effective at the population level over the long term. The Papanicolaou smear test is the most commonly used screening method for cervical cancer. It was first used for mass screening in the 1940s. Other screening methods, such as colposcopy and cervigrams, have been used in the past, but are not widely available or proposed at this time since they have not been thoroughly investigated. Recent years have seen the identification of several effective strategies for cervical cancer prevention. These include cervical cytology using either conventional or liquid-based methods, high-risk (HR) human papillomavirus (HPV) DNA testing, and a variety of iterations of direct visual inspection of the cervix following application of acetic acid (VIA) or Lugol's iodine (VILI). Performance (accuracy and reproducibility), affordability, and ease of integration into screening programmes are all factors to consider when selecting a screening assay (e.g., coverage, acceptability, and single versus multiple visits). There is no screening technique that will be equally applicable in all scenarios, and the right balance between these factors will invariably differ from one country to the next [11].

3.0 CERVICAL (PAP) SMEAR – THE HISTORY REVISITED

According to experts, the Papanicolaou (Pap smear) test is now the most cost-effective cancer prevention and detection programme that has been developed thus far. It is a simplified non-intrusive procedure to examine the cells lining the surface of the cervix for precancerous lesions. The Pap smear test is currently the most extensively used method of avoiding cervical cancer, with screenings occurring once a year to three times a year, depending on the setting. It was coined by George N. Papanicolaou, who discovered that a small sample of cells taken from the cervix can be used to detect damaged cells of the cervix. He published his findings in the journal *Science* [12]. After several years of collaboration with gynaecologist Herbert Trout, Papanicolaou published a book explaining a method for detecting these cells. The technology was developed in partnership with Trout. Studies conducted in the 1940s corroborated Papanicolaou's finding that use of cervical smears enabled not only the detection of malignancies, but also the detection of precancerous changes in the uterine cervix, which were previously undetected. Eventually, the work of Papanicolaou and Trout led to the

implementation of large-scale cervical cancer screening programmes in the late 1950s. On Figure 1, you can see an illustration of the technique for making a PAP-smear as well as an illustration of how a PAP-smear appears when it is observed under a microscope.

In their study, they demonstrated the effectiveness of a routine vaginal smear test for the rapid diagnosis of cervical malignant and precancerous alterations. The standard Pap test is a straightforward procedure that consists of the procedures listed below. The newly created American Cancer Society endorsed the use of the vaginal smear as an effective cancer prevention test for carcinoma of the uterine cervix in 1945, making it more than 50 years after the test was first introduced. Dr. Charles Cameron, the inaugural Medical and Scientific Director of the Society, who also happened to be Dr. George N. Papanicolaou's personal friend and confidant, was the one most responsible for taking this move. Presented during the National Conference on Gynecologic Cancers, held in Orlando, Florida, on April 2-4, 1992, Cameron was the person who arranged the inaugural National Cytology Conference in Boston in 1948, according to the paper. Authors' affiliation: The Department of Pathology, Montefiore Medical Center, Albert Einstein College of Medicine, New York City (Bronx). Originally devised to research the hormonal status of mice, Papanicolaou's sampling technique was a vaginal pool smear, which was the approach that was first applied in clinical observations on women [13].

3.1 THEPAP SMEAR

Initially designed to identify uterine cancer, the PAP smear eventually proved to be beneficial in the early detection of cervical carcinoma in its precancerous state. A spatula and mascara-like brush are used to collect cells from the ecto- and endocervix. The cells are then smeared on a glass plate and instantly fixed in 95 percent ethanol before being air dried. It takes three steps to complete the traditional Papanicolaou staining procedure. The first step is to apply the nuclear stain haematoxylin to the slide, followed by an orange counterstain (Orange G) to stain keratin, and the final step is to apply a turquoise counterstain (Eosine Azure) to stain several other components of the slide. Cytotechnologists and pathologists are the people who should do the interpretation. As part of the clinical gynaecological examination, PAP smears are taken as part of a systematic screening programme and on demand (opportunistic screening).

The standard Pap test is a straightforward procedure that is comprised of the components listed below [14]

The speculum is inserted into the vaginal opening to allow for better viewing of the cervix.

- Sample cells are obtained by brushing or swabbing them into and around the cervix.
- Preservative is applied to the cells in a glass to keep them from deteriorating.
- Using a marker, samples are marked to improve the contrast in the specimen, which will be used to highlight structural patterns for investigation under a microscope in the three labs.

The use of Pap tests (or Pap smears) for cervical cancer screening has resulted in a significant decrease in the mortality rate for women who have been examined on a regular basis in countries that have an effective screening programme. However, the entire process is time-consuming, involves observer bias, and is devoid of quantitative proof that can be replicated. Thus, an

automated approach for Pap smear screening will be of great benefit to pathologists in the field of cancer screening [15]. As a result of its high incidence, possibility for prevention, and lack of an automated system for Pap smear screening, cervical cancer is a disease that requires in-depth research and investigation. Conventional cervical cancer screening can significantly reduce the incidence and mortality of cervical cancer; however, manual analysis of samples is time-consuming, subject to variations in sensitivity and reproducibility, and necessitates the involvement of medical experts in the analysis of the specimens.

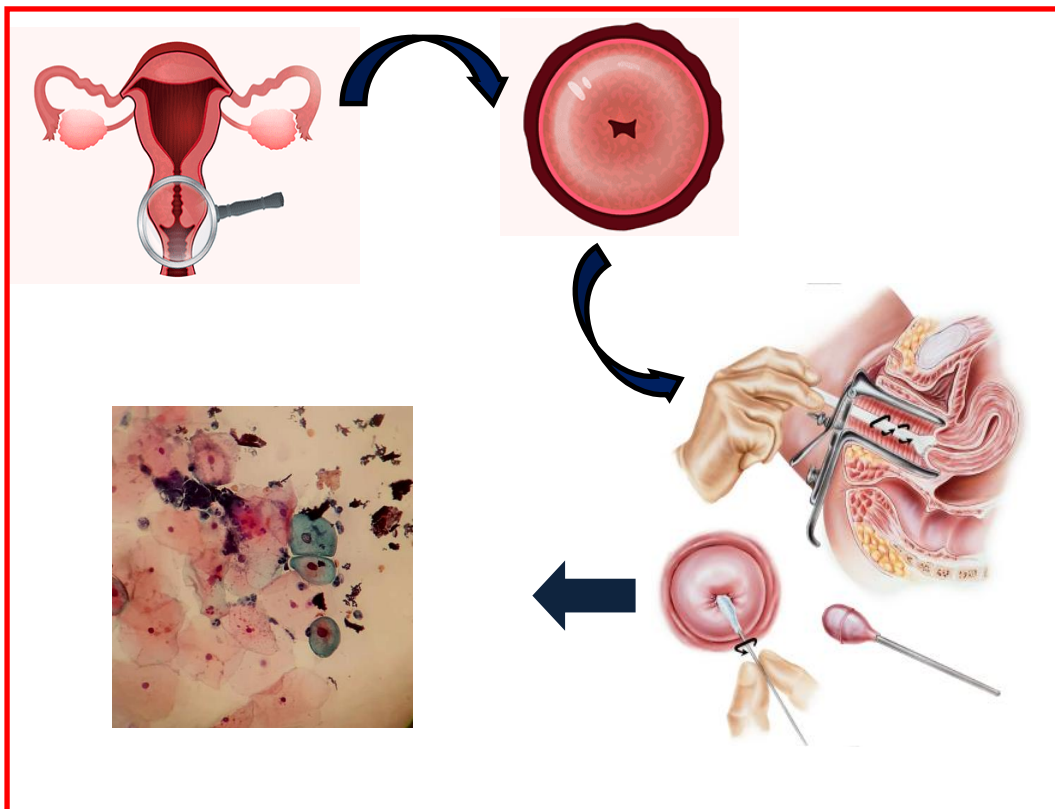


Figure 1 – Diagrammatic illustration of Pap smear test

4.0 LIQUID-BASED CYTOLOGY

Liquid Based Cytology is a new method for sample cell preparation for cytological testing that is similar to pap smear testing. The difference is that instead of smearing the cells in the glass slide, the cells are washed with a preservative liquid solution and then sent to the lab for removal of non-diagnostic materials such as mucus, pus, and blood cells before being sent to the lab. Following the preservation, a thin layer of cell is created on a glass slide, and the cell is viewed under a microscope in the same manner as a typical smear test in the same way [16].

Various LBC preparation processes have been developed in order to produce specimens that are more suitable for both visual and machine examination. When collecting cellular materials from the cervix, a popular method is to soak the brush or spatula with all of the materials in a liquid, which is then processed in various ways before being put onto a glass slide and fixed and stained. A cellular sample that has been disseminated in a monolayer with optimal density over a well-defined portion of the glass slide is, in theory, the desired outcome [17].

There are two major forms of LBC that are commercially available: ThinPrep (Cytoc Corp, Marlborough, MA, USA) and Surepath (Cytoc Corp, Marlborough, MA, USA) (BD, Franklin Lakes, NJ, and USA). The homogeneous spread of epithelial cells in a thin layer makes microscopic interpretation easier, which is why cytotechnologists and pathologists favour this procedure in the majority of instances [18]. Several studies have reported higher sensitivity than that observed in standard PAP smears, while some have questioned the validity of such findings in some cases.

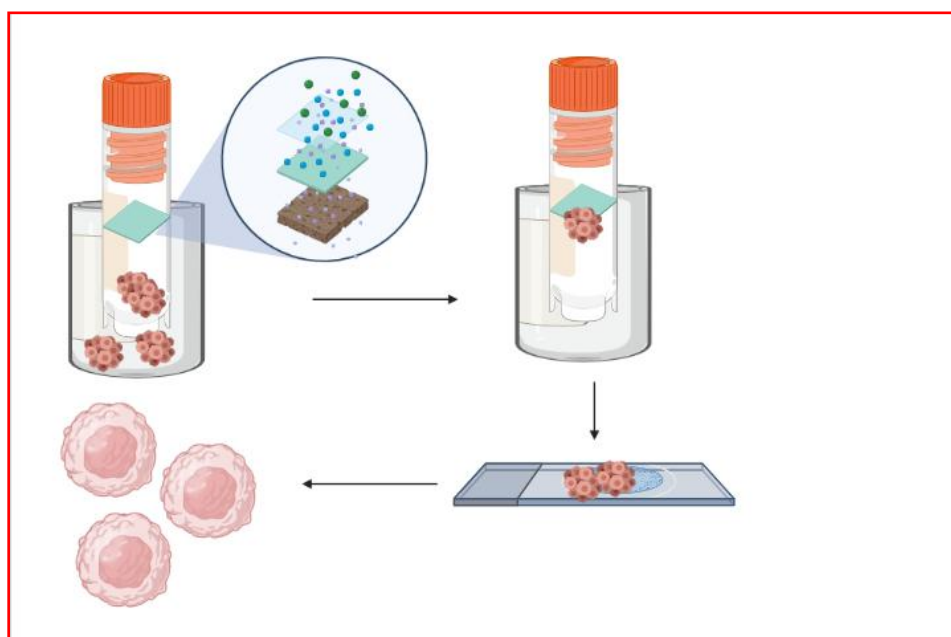


Figure 2 - Schematic diagram highlighting the basic principle of LBC technique. The rapid movement of the filter causes cellular dispersion. Simultaneously negative suction is applied within the vial of filter that helps to remove the fluid and the cell sticks on the filter.

4.1 Advantages of LBC over Conventional Smear

In the case of LBC, the majority of the collected cells are available in the liquid medium of the collection vial, whereas the majority of the collected cells are stuck to the spatula of the convention smear preparation and the cells are thrown into the waste basket in the case of convention smear preparation. Neither air drying nor any other artefacts are present in the LBC preparation. A nearly total absence of blood, mucus, or necrotic debris may be observed in the LBC preparation; in addition, the cells are concentrated in a tiny area that is easy to screen. Certain LBC preparations contain a monolayer of cells that have been prepared in a single layer. It is feasible to do an HPV test on the remaining material from the LBC sample. An automated detection of malignant cells in a smear may be possible with the use of the monolayer cell preparation.

5.0 Machine learning and artificial intelligence in pap screening

Lack of proper access to microscope diagnostics is a concern in low-resource settings, and it makes it difficult to diagnose common and treatable diseases. Researchers have developed computer-aided cervical cancer diagnosis methods for the identification and classification of cancer cells using histology images and for the classification of cancer cells using MRI images [19]. Despite substantial advancements in digital microscopy diagnostics at the point of care (POC), clinical application of these technologies has been delayed. In this section of the review, we will cover a digital diagnostics system in which microscope slides are digitised at the point of care (POC) and uploaded utilising local data networks for analysis with an artificial intelligence model based on deep learning, as well as other topics.

Deep learning-based algorithms have recently been applied to a vast range of medical image-analysis applications, with levels of performance that are on par with or even better than those of human experts in some cases [20]. It is possible that artificial intelligence will aid in the revolutionization of cervical cancer screening, particularly in areas where access to more modern screening methods is limited. According to the National Cancer Institute's Division of Cancer Epidemiology and Genetics, computer analysis of Pap tests under the microscope [cytology] performed better than a human expert reviewer of Pap tests under the microscope [cytology] in identifying precancer.

5.1 Machine learning in cervical cancer screening – How it works?

Machine Learning is the science of computer algorithms that learn and improve on their own as a result of their experiences. Information filtering systems that automatically learn users' interests are examples of machine learning applications. Data mining algorithms that uncover general rules in big data sets are examples of machine learning applications. It is possible to design systems with the help of machine learning, which will result in greater efficiency and effectiveness of the system. The classification technique is one of the most widely used machine learning techniques [21]. A vast amount of information about patients and their clinical histories has been amassed in medical databases throughout the years. Incompleteness, incorrectness, and inexactitude are all possible qualities of data in this format. When it comes to healthcare applications, classification analysis is one of the most extensively used data mining techniques. It is used to assist and improve the quality of medical diagnosis. In medical categorization, all approaches are well-known, and they all rely on prior knowledge of the data that has already been collected. In most cases, a subset of the current dataset is used as the training sample for the classification approach in question. Classification can be accomplished through the use of several data mining techniques.

All of the machine screening systems on the market today are designed to function with liquid-based formulations [22]. It is necessary to scan a cell sample at a sufficiently high resolution in order to accurately extract the features that may be used to evaluate whether it is normal or suggesting a precancerous alteration before it can be analyzed in a computer. Taking up this task is really difficult. An area of 25 50mm will yield 31 billion pixels with 0.2 micron pixels at an

image resolution of 100 percent. Even with the latest high-speed transfer systems, simply transmitting this amount of data from the camera to the computer will take minutes. Given that there are currently no lenses that can resolve the entire specimen area at once and no image sensors with 31 giga pixels, we are faced with the challenge of relocating the lens throughout a large number of image fields that collectively encompass the specimen. Using a high resolution microscope lens with a field of view with a diameter of around 0,5mm, we can capture 5000 picture fields on a 6 megapixel sensor. It will take at least 10 minutes to reposition and take a photo at each of these locations. This can be mitigated by employing constant motion and flash lighting to freeze the images in the camera. The CYBEST4 system was the first screening system to make advantage of this concept, and it was later used in the AutoPAP system as a result. Another option is to employ a 1D sensor with a length of, for example, 2000 pixels and to move the microscope stage smoothly in the orthogonal direction to the camera. This concept was applied to the Cerviscan and Diascanner systems. Despite having a reduced resolution, it is also employed in the currently popular slide scanners by Aperio[23].

5.2 Classification of Cervical Cancer using Artificial Neural Networks

RoyanDawudAldian and colleagues suggest an automatic categorization for normal and pathological cervical cells using artificial neural networks (ANNs) and learning vector quantification (LVQ) (LVQ). The sample data sets are collected, and the procedures in digital image processing such as pre-processing, filtering, and feature extraction are carried out on them using the samples. The input image is stored in the ANN, and the LVQ method is used for the classification of cervical cells for the detection of cancer. The LVQ method calculates the coefficient mean value of the extracted image, which is then used for classifying the normal and abnormal cells with an accuracy of 90 percent. FatemehHodaMoghimi and colleagues offer artificial neural network (ANN) techniques for usage in health clinics, in which a multi-layered perceptron is used in the ANN to map the thinking and key components of the patient. The architecture of an ANN consists of one input layer and one output layer, with no constraint on the number of hidden layers that can be utilized in the algorithm [24].

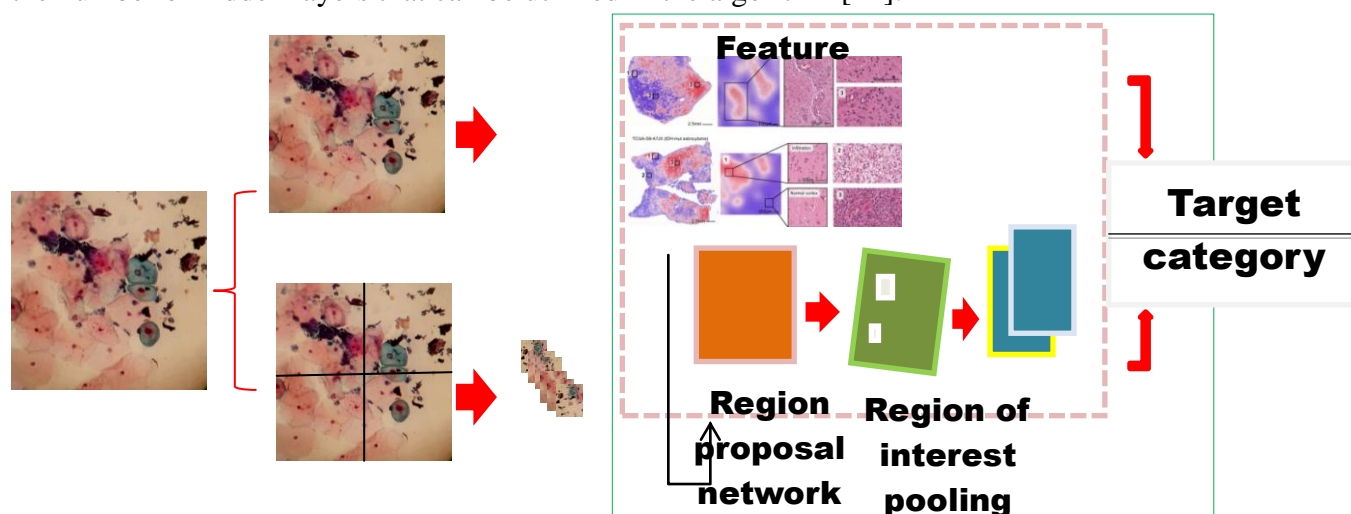


Figure 3 - The suggested convolutional neural network (CNN) system for cervical cancer screening is depicted in this diagram. The feature map is obtained by the convolution network extracting image information, and the target location information is obtained by the proposal network screening the target region based on the feature map. A convolutional classifier was used to identify the diseased cells and their locations based on the feature map and target location. Combining the recognition results of the two networks yielded pathological cell information. The results of the two models are similar.

The artificial neural network (ANN) is employed in all medical applications and can be simply mapped with learning methodologies for better comprehension and results. Phatak and colleagues suggest a new approach for identifying cervical cancer using a support vector machine (SVM) and an artificial neural network (ANN) for the detection of cervical uterine cancer in the cervical cervix. To compare the classification approaches used to detect cervical cancer, SooryPraba and colleagues used neural networks, k closest neighbour, and Bayes classifiers to determine the presence or absence of cervical cancer. The classification of normal and pathological cells is accomplished through the use of three classifiers. The input image is sent into the classification algorithm, which extracts the features that are needed for the classification results. An ANN with three layers is employed, with the input layer, the output layer, and the hidden layer all being used. In this case, the data set is a trained data set, which delivers more accurate results than other types of classifiers [25]. N. Mustafa and colleagues suggest a system based on artificial neural networks for obtaining novel characteristics from cervical cells. The input image is taken from Pap smear slides, and the perimeter, area, red, blue, and green colours, as well as their intensity levels, are recovered. This information is used by the ANN to classify the cervical cells into normal and malignant cells, respectively [26].

6.0 Conclusion

The research examines a number of recent high-profile studies on the automated detection and categorization of cervical cancer from pap-smear photographs. This review should aid field researchers in recognizing the difficulties associated with some of the strategies described, as well as give a solid foundation for building and developing new algorithms or improving existing ones. The significance of the framework built for pathologists to detect cervical cancer cells is discussed in this article. The researchers introduced new automated cancer detection and classification frameworks for reliably detecting and segmenting cell nuclei in Pap smear microscopy images. This is usually the first stage in the creation of an automated cervical cancer screening system based on nucleus characteristics. The researchers introduced a collection of new statistical textural features for assessing nucleus chromatin patterns in cells from traditional Pap smears.

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