

**Clinical application and efficacy evaluation of liquid-based cytology combined with HPV  
testing in cervical cancer screening**



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### Abstract

To detect abnormalities in cervix cells that may result in cancer, cervical cancer screening is performed. A screening might involve testing for the human papillomavirus, cervical cytology, or both. Cervical cancer screenings need to be routine for most women. This research aimed to conduct a clinical analysis of the liquid-based cytology (LBC) cytologic assessment and highrisk human papillomavirus (HPV) utilizing Screening for cervical cancer. 1000 females who visited the patient clinic as study participants were screened for this study. The traditional Pap LBC test was compared to screening with HR-HPV testing for subtypes 18 and additional HR-HPV types and the data was evaluated using SPSS. A total of 1000 women aged 20 to 40 received cervical cancer screening over the research period. 600 underwent screening with LBC between 2020 and 2021 while 400 underwent screening with HR-HPV between 2021 and 2022. Referral rates for colposcopy were higher for HR-HPV testing when compared to primary LBC screening. When compared to LBC screening, the identification of CIN 3+ lesions was greater when using HR-HPV screening. In summary, primary HR-HPV screening must be taken into consideration for screening as it was linked to a greater detection rate of CIN 3+ than cytology screening.

Keywords: Cervical Cancer, Screening, Colposcopies, cervical cytology, human papillomavirus (HPV)

## **1. Introduction**

Cervical cancer screening is an important public health measure aimed closer to the early detection and prevention of cervical cancers. Traditional screening strategies include the Pap smear, which examines cervical cells for abnormalities [1]. However, upgrades in medical era have brought about the improvement of human papillomavirus (HPV) and liquid-based totally cytology (LBC) checking out, which offer superior accuracy and regulation in screening efforts.

### **1.1 Liquid-based cytology (LBC)**

LBC is a contemporary approach wherein cervical cells are accrued and preserved in a liquid medium in advance than being processed for exam [2]. The method complements the excellent of the pattern with the useful resource of decreasing infection and dispensing cells lightly at the slide. LBC has largely changed conventional Pap smears in lots of settings because of its greater sensitivity and ability to stumble on precancerous lesions more successfully. Additionally, LBC for the simultaneous trying out for HPV from the equal pattern, growing the convenience for sufferers and performance in laboratories. The progressed pattern additionally reduces the charge of unsatisfactory specimens, leading to greater reliable diagnostic consequences [3].

### **1.2 HPV testing**

HPV testing includes detecting the presence of excessive-hazard HPV strains recognized to cause cervical most cancers. HPV is a common sexually transmitted contamination, and positive traces are strongly associated with the development of cervical cancers [4]. By detecting those excessive threat traces, HPV testing allows satisfying women based on their threat of developing cervical cancers, allowing for extra centered observe-up and control. This stratification allows clinicians to prioritize sufferers who want on-the-spot intervention and presents reassurance for those in low danger. Furthermore, everyday HPV testing can help to track the effectiveness of vaccination applications geared toward reducing the superiority of excessive-danger HPV traces [5]. As extra females undergo HPV testing, public fitness statistics will improve, main to better-informed regulations and preventive strategies.

### **1.3 Combined screening approach**

Combining LBC with HPV testing, also known as co-testing, gives a complete cervical cancer screening method. This dual method capitalizes on the strengths of both strategies and the morphological assessment of cervical cells through LBC and the molecular detection of high-chance HPV strains [6]. Co-testing has been shown to increase the detection rate of significant cervical lesions, thereby enhancing the overall effectiveness of screening programs. Co-testing can lead to advanced intervention and remedy, improving the affected person's outcomes. It additionally gives a higher reassurance level of females who check terrible on both tests, as their danger of growing cervical cancer is appreciably lower. Ultimately, the approach supports extra personalized and specific patient care in cervical cancer prevention [7].

### **1.4 Efficacy and benefits**

It has demonstrated that the combination of LBC and HPV testing has superior sensitivity and negative predictive value compared to either method [8]. This combined approach identifies the increased incidence of cervical intraepithelial neoplasia (CIN) and cervical cancer at an earlier stage but allows for extended screening intervals in females who do not test positive for HPV and LBC reducing the frequency of unnecessary procedures and associated costs [9].

The integration of liquid-based cytology and HPV testing represents a significant advancement in cervical cancer screening. Its ability to locate an extra variety of high-danger instances and provide long-term safety makes a valuable device in the fight in opposition to cervical cancers [10]. It continues to validate its efficacy and fee-effectiveness, it's miles possible that extra healthcare systems worldwide will adopt this combined approach, eventually resulting in a decline for both prevalence and mortality of cervical cancer [11].

### **1.5 Aim**

The purpose of this paper is to analyze the screening including liquid-based cytology (LBC) cytologic assessment between 2020 and 2021 and high-risk human papillomavirus (HPV) between 2021 and 2022 utilized for cervical cancer.

### **1.6 Organization**

The remaining part of the paper is Part 2 provides the related work, Part 3 presents the methods and materials, Part 4 represents the result and discussion and Part 5 discusses the conclusion of the paper.

## **2. Related work**

Study [12] assessed the usefulness of the ThinPrep cytologic screen and the HPV co-test for detecting cervical cancer during pregnancy. The findings highlighted the potential for greater specificity in cervical cancer detection when carrying a child and imply that HPV evaluation, in conjunction with cytology, offered an effective screening method for expectant mothers or either alone. The HPV16/18 group's noticeably higher frequency of HSIL+ highlights how crucial it was to consider genotype-specific factors.

Study [13] compared cytology with the effectiveness of a seven-type HPV messenger ribonucleic acid (mRNA) test. Five percent of people tested positive for HPV-Deoxyribonucleic acid (DNA), and ninety-seven percent of people obtained accurate HPV mRNA findings. Thirty-five percent of the sample had an elevated HPV mRNA test, while fifty-five percent of the sample showed abnormalities in cytology. The benefits and drawbacks of screening could be more evenly distributed if such a biomarker were used as the colposcopy threshold.

The effectiveness of visual inspection with acetic acid (VIA) and LBC with the results of histopathological analysis was compared in study [14]. In the experiment, a highly significant sample of women had examinations by VIA and LBC. Additionally, samples of tissue from individuals who tested positive for VIA and unusually positive for LBC were obtained. The finding of the research LBC changed into a better option for inspecting cervical cytology than a standard Pap test.

Research [15] assessed the clinical assistance of extended HPV sequencing in dangerous HPV-high-quality women's triage, with a focus on the compromises between referrals for a colposcopy and genital precancer sickness recognition. According to the experiment, extended HPV sequencing may be employed as a triage strategy that has been combined into HPV-based totally cervical most cancers checking out. It could decrease the need for referrals for colposcopies while maintaining powerful hazard stratification and comparable ailment detection.

The efficiency of an HPV-DNA and the cervicovaginal smear (CVS) co-test were assessed in study [16]. A retrospective analysis looked at the pathological outcomes of 225 woman patients who had either CVS or colposcopic vaginal biopsies after receiving HPV-DNA screening with CVS. The conventional smear method worked well for identifying high-grade tumors. The findings emphasized the importance of checking out to save you needless treatments and to increase appropriate comply with-up methods, no matter the constraints of the experiment.

In an early age range of 25–30 years old, the objective was to compare the outcomes of two screening techniques with regard to the identification rate of high-grade female intraepithelial lesions presented in study [17]. During a single screening round, historical information on cervical cellular biology, hrHPV tests, colonoscopy recommendations, and histological findings were obtained. When it comes to women in the 25–30 age range, primary hrHPV testing should be given consideration as it has been associated with greater identification of cervical intraepithelial neoplasia (CIN 3+) when compared to histologic screening.

Study [18] assessed the cost-effectiveness of AI-assisted LBC analysis for basic cervical cancer detection in comparison with traditional HPV-DNA and LBC testing. To replicate the evolution of tumor growth, an ensemble of women over the course of their lifetimes who were all 30 years old. If the HPV-DNA test's generator cost were marginally less or if AI-assisted LBC was more expensive than traditional LBC, then the most economical course of action would be to conduct an HPV-DNA examination once every five years.

A retrospective evaluation of 428 individuals who had a female biopsy was done to determine the clinical use of high risk (HR)-HPV DNA in conjunction with LBC in a colposcopy of cervical cancer was evaluated in study [19]. To ascertain if patients have persistent lesions, pathological biopsy findings serve as the standard of excellence. Patients who received a positive outcome for the standard were enrolled in the experimental group. As symptoms increased, it was anticipated that the positive result rate for liquid-performed cytology would rise.

Study [20] assessed the outcomes of HPV and LBC evaluating the previous contest to cervical cancer (CxCa) and precursor's diagnosis in a broad population. A laboratory's examination of 9-year contest data demonstrated the usefulness of the LBC component of co-testing. It demonstrated that, in comparison to LBC or HPV alone under testing, testing improved testing for the detection of CxCa in 30 years of age and older females.

Study [21] compared a readily accessible amplification of the DNA HPV test to standard cytology performed with liquids in women 50 years of age and older. Participants were monitored for 64–76 months. Both cytology performed with liquids and the Cobas 4800 HPV genetic test were used to analyze the samples. Five incidences of gynecological carcinoma other than cancer of the cervical cavity were missed by HPV testing at the start. Five cervix tumors were found, two were missed initially by screening for HPV and two by liquid-based cytology.

Article [22] evaluated cervix pap test evaluation using cytology performed with liquids in comparison with traditional cytology. Eighty-four females between the ages of eighteen and sixty who complained of excessive vaginal discharge, among other symptoms, were included. Specimens were considered for both cytology using liquids and traditional pap smears, after which colposcopic-assisted biopsies were accomplished. LBC was superior to the Conventional Pap test for the detection of cervical lesions that were preinvasive.

## **2.1 Problem statement**

The current aspects of cervical cancer screening offer several challenges and opportunities for improvement. Variability in screening methodologies, such as LBC, high risk HPV checking and their combinations, underscores the need for standardized protocols and evidence-based hints. Studies highlight the ability blessings of HPV trying out, especially along with cytology, for more desirable specificity and early detection of cervical lesions during pregnancy and in various age organizations. However, discrepancies in diagnostic accuracy and value-effectiveness across one-of-a-kind screening modalities persist, influencing scientific decision-making and patient effects. Addressing these issues we analyze the screening include LBC and high risk HPV for cervical cancer to improve prevention efforts and improving the detection quotes of precancerous lesions and cancers.

## **3. Methods and materials**

In this section, we discuss the participants involved in the experiment and provide a comprehensive explanation of the initial screening examination along with the data statistically. We examined, using the experimental method, the data for all women aged 20 to 40 who underwent cervical cancer screening during the next two screening times including liquid-based cytology (LBC) cytologic assessment and high-risk human papillomavirus (HPV).

To prevent the period of transition bias, researchers permitted a one-month break between the two periods. Data from the past on histologic findings, referrals for colposcopies, HR-HPV testing, and cervical cytology were obtained. Women whose samples were classified by the healthcare professional who collected them as a diagnostic test because of illnesses or other medical fears, and not a screening test, were not allowed to participate in the study. Every three years, HR-HPV negative women receive referrals for standard screening. Reactive cytology results were not relevant in the referral process for a colposcopy for women who tested positive for type 18 HR-HPV. For females who had confirmed test results for non-18 high risk of HPV and whose cytology showed > aberrant squamous cells of unknown significance (ASCUS), an abdominal ultrasound was also advised.

It was recommended to repeat HR-HPV and cytology tests in eleven months if the histology results were normal. Irrespective of the reflexive biopsy result, the women were recommended for a colonoscopy if the HR-HPV test maintained positive after a year. Results of anomalous abnormalities were categorized as high or low-level cervical cytology findings in the database. Atypical squamous cells of undetermined significance (ASCUS) have been included in minimal cervix histology. Anomalous glandular cells (AGC), atypical squamous cells that cannot rule out high-grade squamous intraepithelial lesions (HSIL) (ASC-H), and HSIL were all included in high-level cervical cytology.

Women with aberrant morphology or rarely, ASCUS were directed for a colposcopy throughout the first LBC testing phase. Women who reacted highly for additional high risk HPV with weak cytoplasmic or who scored positive for high risk HPV 18 during the first round of testing were encouraged to inquire about a colonoscopy despite the cytologic results. The medical professional decided whether to proceed with colposcopically assisted samples if abnormal alterations were seen during the colposcopic examination. Colposcopy-guided samples' histopathology reports were gathered after the pathological screening test outcomes. The HR-HPV screening group's female members were monitored, and those in the LBC group were monitored. Premalignant and cancerous lesion identification rates, morphology results, and colonoscopy referrals have been compared between HR-HPV-based and cytology-based screening procedures. We utilized CIN3+ detection rates as our primary endpoint since women under 40 had relatively high recurrence rates of CIN 2.

### **3.1 Initial screening examinations**

The cervix samples were gathered using Hologic fluid tubes. Tests for HR-HPV DNA and cytology were conducted on identical samples. Prior to examination, the specimens were kept at ambient temperature for a maximum of six weeks. First, DNA was extracted utilizing a computerized Cobas 480x apparatus, and then real-time quantitative testing was performed using a Cobas 480z device. In two independent assays on the same sample, the test finds 14 different kinds of high risk HPV, findings for types 18 and the remaining types, which are aggregated without particular genetic distinguished standings are obtained separately.

### **3.2 Examining data statistically**

The SPSS software was used to analyze the data. When a screening test is positive and additional clinical therapy in accordance with the suggested procedure is required, we characterize it as positive. Category-specific variables were subjected to the Chi-square test. The odds ratios for the variations between testing and high risk HPV were determined, along with their respective ranges of confidence. A value of  $p < 0.04$  was deemed to be statistically significant.

## **4. Result and discussion**

We used 1000 females aged 20-40 in this experiment and separated them for each screening. 600 women for LBC screening and 400 women for high risk HPV screening.

### **4.1 LBC screening**

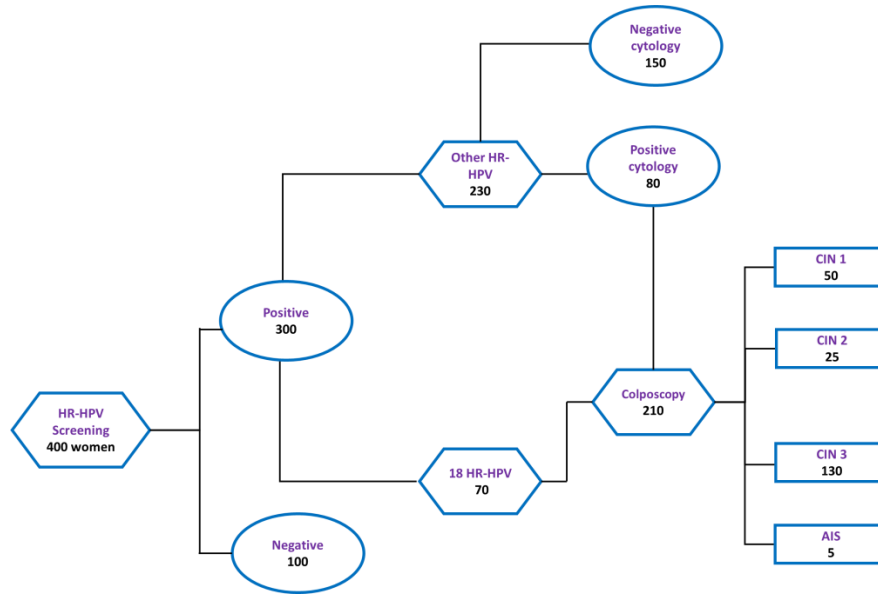
Figure 1 displays the structure of LBC screening. In Figure 1, Out of 600 people who underwent Liquid-Based Cytology (LBC) screening, 200 received bad consequences, indicating no signs and symptoms of abnormalities. The remaining four hundred people acquired positive outcomes, suggesting the presence of abnormalities that required further analysis. Those 400 people with tremendous results, 275 proceeded to undergo colposcopy, an in-depth examination to similarly check out the abnormalities. The colposcopy results confirmed that amongst these 275 people, 70 had been diagnosed with CIN 1, 30 with CIN 2, and 100 with CIN 3.



**Figure 1:** Structure of LBC screening

## 4.2 High risk HPV screening

Figure 2 represents the architecture of HPV screening. In this screening, we used 400 women, 100 received negative, and 300 received positive. Among the positive group, 70 females are dominant, particularly for high risk HPV 18 and 230 females for other high risk HPV (non-18). Further of non 18 separate two groups including positive and negative cytology. 80 females for positive cytology and 150 for negative cytology. The 18 HPV and positive cytology include colposcopy for 210 women who undergo CIN 1 (50), CIN 2 (25), CIN 3 (130), and AIS (5). This structured technique enables to detection and management the females in different stages of cervical cancer and focused intermediations and follow-up based on the unique screening.



**Figure 2:** Architecture of high risk HPV screening

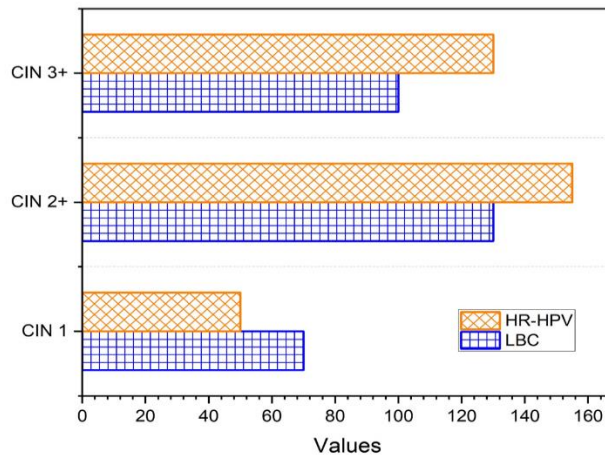
### 4.3 CIN detection

Table 1 displays the CIN calculation of both screening tests with p-value. We only consider positive cases in both screenings. It illustrates the number of positive cases found by HPV and LBC screening, with P values less than 0.001 indicating statistically significant differences. The study emphasizes the noteworthy prevalence of HPV 18 by differentiating patients positive for HPV 18 from those positive for other high risk HPV kinds. The classification of cervical cytology results into three categories. Low-level, Abnormal, and High-level findings describe the range of abnormalities found by cytological analysis. CIN is further classified into levels based on the results of colposcopy, cases classified as CIN 2+ and CIN 3+ represent distinct levels of disease intensity. In general, the table offers a thorough overview of screening results and diagnostic associations, which is crucial for comprehending the frequency and consequences of cervical health problems in the tested population. Regarding the findings, the HPV screening is greater in CIN 3+ compared to LBC screening. Figure 3 displays the outcomes of colposcopy in LBC and HPV screening.

**Table 1:** CIN calculation of both screening tests with a p-value

|                | LBC screening | HPV screening | P values |
|----------------|---------------|---------------|----------|
| Positive cases | 400           | 300           | <0.001   |

|                   |     |     |        |
|-------------------|-----|-----|--------|
| HPV 18            | IR  | 70  | <0.001 |
| HPV non 18        | IR  | 230 | <0.001 |
| Cervical cytology |     |     |        |
| Low-level         | 90  | 70  | <0.001 |
| Abnormal          | 150 | 130 | <0.001 |
| High-level        | 50  | 65  | <0.001 |
| Colposcopy        |     |     |        |
| CIN 1             | 70  | 50  | <0.001 |
| CIN 2+            | 130 | 155 | <0.001 |
| CIN 3+            | 100 | 130 | <0.001 |

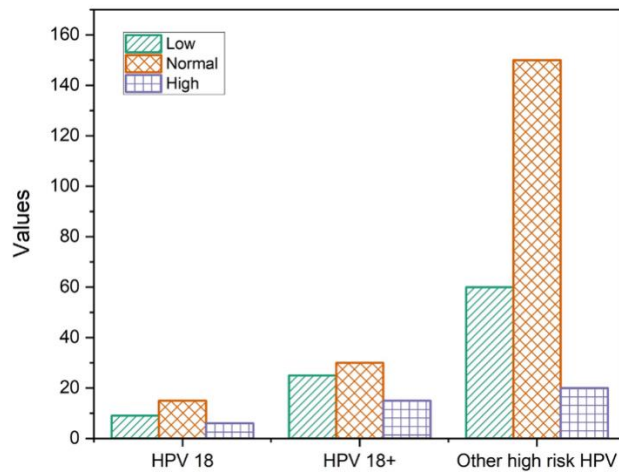


**Figure 3:** Outcome of colposcopy in both screening

Table 2 and Figure 4 represent the cytology outcomes for HPV 18 +, 18 and other high risk HPV (non-18). In the table, participants are categorized in step with the forms of HPV located (HPV 18, HPV 18, and Other high-hazard HPV) in addition to their cytology consequences (Low, Normal, and High). It denotes who is healthy into a positive aggregate of HPV and cytology classes. In low level cytology, 9 females in HPV 18, 25 females in HPV 18+ and 60 females in non-18. At the Normal level are 15 females for HPV 18, 30 females for HPV 18+, and 150 for non-18. At last, high level cytology has 6 females for HPV 18, 15 females for HPV 18+, and 20 for non-18. According to that, other high risk HPV have a high amount of cases compared to others.

**Table 2:** The cytology outcomes for HPV 18, 18 +, and other high risk HPV (non-18)

| Cytology | HPV 18 | HPV 18+ | Other high risk HPV (non-18) |
|----------|--------|---------|------------------------------|
| Low      | 9      | 25      | 60                           |
| Normal   | 15     | 30      | 150                          |
| High     | 6      | 15      | 20                           |



**Figure 4:** Outcomes of cytology for HPV 18, 18 +, and non-18

Comparing women affected by non-18 high risk HPV types to those with HPV 18 transmission, Table 3 shows women with abnormal cytology and CIN 3+ lesions were detected. We analyzed normal and abnormal in HPV 18 and HPV 18+. A considerably higher probability of CIN 3+ was linked to HPV 18 infected with abnormal cytology as opposed to HPV 18 infected with negative cytology ( $p < 0.001$ ). Consequently, a significantly greater rate of CIN 3+ ( $p < 0.001$ ) has been related to concurrent infections of HPV 18 with non-HPV 18.

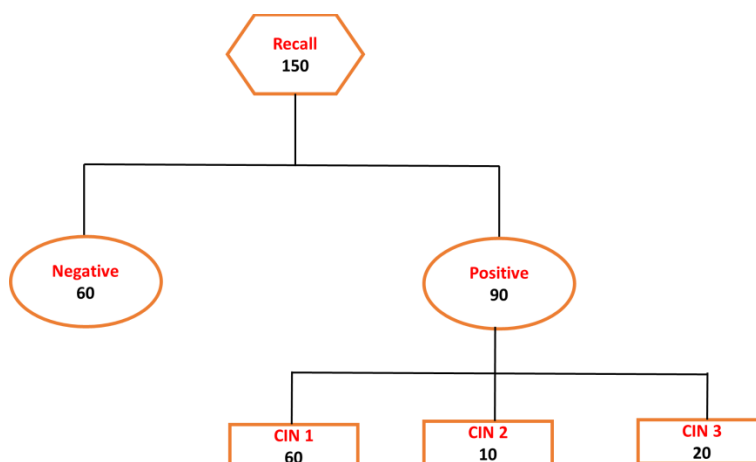
**Table 3:** Colposcopy-guided samples yield histopathology by infecting the primary HR-HPV screening category's cytology and HPV genotype

| HPV | HPV 18 | HPV 18+ | Other high risk HPV |
|-----|--------|---------|---------------------|
|-----|--------|---------|---------------------|

| Cytology          | Normal | Abnormal | Normal | Abnormal | Abnormal |
|-------------------|--------|----------|--------|----------|----------|
| Amount of females | 12     | 18       | 90     | 100      | 230      |
| CIN 1             | 2      | 5        | 23     | 25       | 60       |
| CIN 2             | 3      | 2        | 15     | 18       | 20       |
| CIN 3             | 7      | 10       | 45     | 55       | 130      |
| AIS               | 0      | 2        | 0      | 0        | 0        |
| CIN 2+            | 10     | 12       | 60     | 73       | 150      |
| CIN 3+            | 7      | 10       | 45     | 55       | 130      |

#### 4.4 Screening for recall

In the time frame of the initial screening, about 150 women with normal cytology and other non-18-hour HPV results were advised to return for highrisk PV assessment and monitoring cytology within a year. 150 of them had recall hour HPV screening during the research period. The study protocol's detection rate of high risk HPV and CIN is shown in Figure 5. After three years, 60 women who had recovered from their infection were referred for standard high risk HPV screening. The remaining ninety women were recommended for a colposcopy due to their ongoing high risk HPV infection. In the positive recall group (341 days) and the one with a negative recall group (320 days), the median time to recall assessment was similar. In total, recall testing identified 20 additional women with CIN 3+ who had normal original cytology results.



**Figure 5:** Screening for recall

## **5. Conclusion**

Cervical cancer screening identifies anomalies in cervix cells that may lead to cancer. Testing for cervical cytology, the virus that causes cervical cancer, or both may be part of a screening. For most women, regular tests for cervical cancer are essential. In this paper, we analyze LBC screening and high risk HPV screening for cervical cancer. We used 1000 women in this experiment, 600 for LBC screening and 400 for high risk HPV screening. A focus on comparing traditional PAP LBC assessments to screening with high-risk HPV testing, along with HPV subtypes 18 and different excessive-danger sorts is the usage of SPSS for analysis. Thousand girls aged 20 to 40 underwent cervical cancer screening. Of these, six hundred were screened for the usage of LBC from 2020 to 2021 while 400 underwent HR-HPV screening from 2021 to 2022. Results confirmed that referral rates for colposcopy have been higher with HR-HPV testing in comparison to primary LBC screening. Importantly, HR-HPV screening identified a notably wide variety of CIN3+ lesions as compared to LBC screening. Because the primary HR-HPV screening detects CIN 3+ more accurately than cytology-based screening methods, these results support the use of this method for cervical cancer screening.

### **5.1 Future scope and limitation**

The consequences' generalization can be impacted with the aid of the examination's historical scope, which might no longer have captured long-term consequences or modifications to screening protocols over time. The use of SPSS for facts analysis, which might also omit complicated subjective factors in screening consequences, maybe another disadvantage. Finally, differences within the interpretation and degree of reveal in of clinicians when referring sufferers for colposcopy might also result in variances in the accuracy of the analysis and the remedy alternatives that follow. Future studies may investigate how to incorporate it into cervical cancer screening programs. Furthermore, research on patient compliance and cost-effectiveness with various screening modalities such as cytology and combined HPV testing may shed light on how best to implement screening protocols.

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