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**Original Article**

# Diagnostic Accuracy of Visual Inspection of Cervix Using Lugol's Iodine for Detecting Cervical Carcinoma taking Histopathology as a Gold Standard

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## ABSTRACT

Cervical cancer arises from the transformation zone of the cervix. Diagnosis is usually made by screening later confirmed by a biopsy. In low resource setups, where modern methods are not suitable, an alternate method is to inspect the cervix with naked eye after applying Lugol's iodine as it highlights the precancerous lesions. **Objective:** To look for the diagnostic accuracy of visual investigation of cervix using lugol's iodine (VILI) for detecting the cervical cancer taking histopathology as a gold standard. **Methods:** Cross sectional study was conducted at Obstetrics and Gynecology department, Services Hospital, Lahore for six months from 1st July 2021 to 31st December 2021. 150 patients were examined using lugol's iodine solution and then underwent colposcopy to determine the diagnostic accuracy of lugol's iodine in cervical carcinoma while setting histopathology as a gold standard. **Results:** The mean age of the patients was 42.11 ± 10.12 years. 8.67% patients were nulliparous, 13.33% registered patients were with parity one, 38.67% patients with parity two, 29.33% patients were with parity three and 10% patients were para four. The sensitivity, specificity, and diagnostic accuracy of VILI was found to be 92.59%, 93.75% and 93.33% respectively, taking histopathology as gold standard. **Conclusions:** According to results of our study we can say that the visualizing the cervix using lugol's iodine (VILI) can be used for detection of cervical cancer.

## INTRODUCTION

The rising burden of malignancies in low & medium-income countries is worrisome [1]. Cervical cancer is the third most common cancer across the globe and it poses great risk to population. The disease burden of cervical cancer varies across the globe, but it is more prevalent in developing countries as compared to developed countries. Cervical cancer among the developing countries is second most common, and 9th most common malignancy globally [2]. Cervical carcinoma is 3rdin place in terms of incidence in females of Pakistan making it a burden on healthcare system [3]. Despite the importance of cervical cancer for public health, the risk of the disease and death from it are still largely out of control since most poor nations lack effective preventative programs [4]. Primary prevention and early detection are two methods for preventing cervical cancer. As a result of screening, early identification, and treatment, the incidence of cervical cancer has reduced in developed countries. However, because of their advanced development, 80% of cervical malignancies in developing nations are incurable at the time of discovery [5]. Cervical carcinoma offers us plenty of possibility for early detection and therefore a significantly improved prognosis because of its sluggish evolution from pre-cancerous lesion to malignancy and easy accessibility to inspection. Early detection may be achieved by systematic screening programs or opportunistic assessment of women visiting outpatient clinics [6]. In low resource countries, a good cancer control approach is through screening and early diagnosis of cancer and pre-cancerous lesions. It being 3rd most

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frequent cancer in our country needs urgent intervention [7]. Timely detection through human papillomavirus (HPV) testing and visual inspection of cervix are very effective and reliable approaches [1]. As cytology-based screening is main stay screening protocol in developed countries. In developing countries, visual inspection of cervix can be an alternative for cervical cancer screening and these programs should be incorporated in national screening programs [4]. Eradicating the cervical cancer is practically unrealistic and applying HPV and molecular testing to LMICs is a bad choice given the heavy burden on the economy of these countries. So, an approach suitable to resources should be planned [8]. The annual deaths due to late detection are increasing in Asia pacific region that too due to late detection. We aimed to conduct this study to confirm whether VILI is reliable tool for early assessment of cervical cancer [9]. It was accessible in areas where surgical or biopsy facilities were not available. Moreover, restricted local studies have been done to assess the accuracy of VILI. Through this study we wanted to gain local magnitude also. This study helped us in improving our screening practice and improve local guidelines for detecting the cervical cancer at an early stage.

## METHODS

A Cross-sectional study was conducted in department of obstetrics and gynecology of services hospital for 6 months from 1st July 2021 to 31st December 2021. After written consent 150 cases who fulfilled the inclusion criteria were enrolled in this study following non-probability, consecutive sampling. Sample size of 150 cases was calculated with 95% confidence level, 15.5% margin of error and taking expected percentage of cervical cancer i.e., 33.5% and taking sensitivity and specificity of VILI i.e., 72.7% and 89.6% respectively for detection of cervical cancer taking histopathology as gold standard. Ethical approval for this study was taken from IRB of the hospital. Females of age ranging from 25 to 60 years, with suspicion of cervical carcinoma, were enrolled in this study. Cervical carcinoma was suspected due to having repeated vaginal discharge i.e., >2 episodes even after 14 days treatment with metronidazole, intermenstrual, post-coital and post-menopausal bleeding. Women who underwent hysterectomy, pregnant females, diagnosed or treated cases of CIN or Cervical cancer, active bleeding from vagina or cervical growth, females who are not sexually active, women with diabetes and hormone replacement therapy were excluded. Demographic data was collected. Visual examination using Lugol's iodine was done with application of Lugol's iodine (VILI). Patients labeled as positive or negative (as per operational definition). All procedures were done by researcher herself. Then females underwent colposcopy leading to biopsy for histopathology by a single surgical team. Reports of histopathology were assessed and compared with results of Visual examination with Lugol's iodine. All this information was recorded in pre-designed proforma. Data were collected then entered and analyzed by SPSS version 20.0. Age being the quantitative variable was calculated as mean and standard deviation. Qualitative variables like symptoms, parity and cervical cancer on Lugol's iodine and histopathology was calculated as frequency and percentage. A 2x2 table was made to know the sensitivity, specificity, positive predictive value, negative predictive value in order to find out the diagnostic accuracy of Visual examination with Lugol's iodine taking histopathology as gold standard. Data was stratified for parity. Post-stratification, chi-square was applied. p-value ≤ 0.05 as significant.

## RESULTS

Cervical malignancy was diagnosed positive by VILI in 56(37.3%) patients, and it was diagnosed negative in 94(62.7%) patients (Table 1).

| VILI | Frequency (%) |
|---|---|
| Positive | 56 (37.3) |
| Negative | 94 (62.7) |
| Total | 150 (100) |

**Table 1:** Frequency distribution of VILI

| VILI | Histopathology | | Total |
|---|---|---|---|
| | Positive | Negative | |
| Positive | 50 | 6 | 56 |
| Negative | 4 | 90 | 94 |
| Total | 54 | 96 | 150 |
| Sensitivity | 92.59% | Specificity | 93.75% |
| PPV | 89.29% | NPV | 95.74% |
| Diagnostic accuracy | 93.33% | | |

**Table 2:** Comparison of VILI with histopathology

The mean age of the patients was 42.11 ± 10.12 years with minimum and maximum ages of 25 and 60 years respectively. Results showed that in patients below 45 years the VILI diagnosed positive cervical malignancy in 32 cases in which histopathology also diagnose positive malignancy in 26 cases. Similarly in above 45 years patients the VILI diagnosed positive cervical malignancy in 24 cases and all the 24 cases were also diagnose positive by histopathology. A highly significant difference, if seen statistically, was noted between the comparison of VILI and histopathology stratified by age. i.e., p-value = 0.000, 0.000 respectively (Table 3).

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| Age (years) | VILI | Histopathology | | Total | p-value |
|---|---|---|---|---|---|
| | | Positive | Negative | | |
| < 45 | Positive | 26 | 6 | 32 | 0.000 |
| | Negative | 0 | 57 | 57 | |
| ≥ 45 | Positive | 24 | 0 | 24 | 0.000 |
| | Negative | 4 | 33 | 37 | |
| Age | | <45 years | | ≥45 years | |
| Sensitivity | | 100% | | 85.7% | |
| Specificity | | 90.5% | | 100% | |
| PPV | | 81.3% | | 100% | |
| NPV | | 100% | | 89.2% | |
| Diagnostic accuracy | | 93.3% | | 93.4% | |

**Table 3:** Comparison of VILI with histopathology stratified by age

In this study, cervical malignancy was diagnosed positive by histopathology in 54(36%) patients, and it was diagnosed negative in 96(64%) patients (Figure 1).

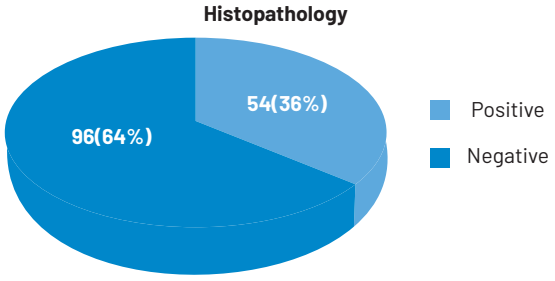


**Figure 1:** Frequency distribution of histopathology

The study showed that in nil or zero parity patients. The VILI diagnosed positive cervical malignancy in 9 cases in which histopathology also diagnosed, positive malignancy were present in 3 cases. Similarly, in multipara patients the VILI diagnosed positive cervical malignancy in 47 cases and all the 47 cases were also diagnose positive by histopathology. Statistically, significant difference was found between the comparison of VILLI and histopathology stratified by parity i. e p-value = 0.015, 0.000 respectively (Table 4).

| Parity | VILI | Histopathology | | Total | p-value |
|---|---|---|---|---|---|
| | | Positive | Negative | | |
| ≤1 | Positive | 3 | 6 | 9 | 0.015 |
| | Negative | 0 | 24 | 24 | |
| >1 | Positive | 47 | 0 | 47 | 0.000 |
| | Negative | 4 | 66 | 70 | |
| Parity | | ≤1 | | >1 | |
| Sensitivity | | 100% | | 92.2% | |
| Specificity | | 80% | | 100% | |
| PPV | | 33.3% | | 100% | |
| NPV | | 100% | | 94.3% | |
| Diagnostic accuracy | | 81.8% | | 96.6% | |

**Table 4:** Comparison of VILI with histopathology stratified by parity

## DISCUSSION

Cervical cancer is a potentially preventable cancer. Global disease burden is enormous costing both money and human resources across the globe with 90% of death due to cervical carcinoma occurring in LMICs [10]. Cervical cancer always develops from a precancerous lesion taking around a decade to convert from premalignant to malignant lesion. The key in improving survival rate is early detection and treatment at pre-malignant stage having almost 100% survival rate as compared to almost one third of that if detected at advanced stage. It was tried to devise a framework for cancer elimination and was concluded that HPV vaccination and screening with VIA or VILI HPV testing and thermocoagulation were effective ways [11]. In China, a meta-analysis consisting of 6 studies was carried out involving 2817 patients. The study concluded that Folate receptor mediated staining solution detection could be used for the screening of cervical cancers in low resource settings [12]. In another study carried out in China, it was found that testing the HPV DNA 3 or 5 yearly or Liquid based cytology 3 yearly and HPV + LBC 5 yearly could be a dominant step, but cost effectiveness can be a big barrier in low resource settings [13]. In Bouvard *et al.*, study found that the pooled sensitivity of VILI was 88% and specificity was 86% VILI appeared to be most useful [6]. Another study carried out on 654 patients who were randomized to undergo VIA or VILI, the positive test rate for VILI was 30.6% and 11.5% were having CIN2+. The sensitivity was 84.2% and specificity was 76.4% with PPV of 31.7% and NPV of 97.4% [14]. Bryan *et al.*, has reported the sensitivity and specificity of VILI ranged from 66.7% - 100% and 71.9% - 91.1% [15]. In Aoki *et al.*, study VILI was found to have a pooled sensitivity of 88% and pooled specificity of 86%. VILI was more sensitive to VIA with equal specificity [16]. 73% sensitivity of VILI and 100% when combined with Pap smear, and specificity of 90.6% of VILI alone and 91.7% when combined with pap smear stated in literature [17]. So, Catarino *et al.*, study has reported that VILI is a good and reliable alternative to interventional investigation methods. Moreover, it was non-invasive and time and cost effective [18]. Pimple *et al.*, found that low cost screening tools are operationally feasible with reduced procurement cost [19]. Total eradication was though financially and practically unrealistic [20].

## DISCUSSION

According to results of our study we can say that the visual inspection of cervix with lugol's iodine (VILI) can be used for detection of cervical cancer in place histopathology, because it has the high sensitivity, specificity and diagnostic accuracy.

## Conflicts of Interest

The authors declare no conflict of interest

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