



**ORIGINAL RESEARCH PAPER**

**Medical Science**

**EVALUATION OF THE ACCURACY OF PAP SMEAR TEST AND COLPOSCOPY IN DETECTING HIGH GRADE LESIONS BEFORE AND AFTER EXCISIONAL TREATMENT.**

**KEYWORD:** Pap smear test, Colposcopy, Sensitivity, Specificity, LEEP

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**ABSTRACT**

**BACKGROUND:** The present study aimed to investigate the accuracy of Pap smear test and colposcopy to identify cervical precancer before and after treatment of high-grade SIL (CIN2+)

**METHODS:** The medical records from 613 women, who underwent excisional treatment of the cervix (LEEP) In the Georgian National Screening Center were reviewed. In this group of patients, histologically confirmed CIN2+ was observed in 285 women. The definition of residual/recurrent disease during follow-up was biopsy-proven CIN2 or worse detected in a punch or re -LEEP specimen. Women with at least two consecutive negative cytology smears and normal colposcopy findings were considered negative for residual/recurrent lesions. In all cases, a conventional Pap smear test and colposcopy were performed. The criterion standard of test accuracy was the histologic report of LEEP specimens and biopsies. Results were compared by statistical analysis.

**RESULTS:** Using a disease threshold of HSIL accuracy of Pap smear test and colposcopy prior to the excisional treatment revealed Pap: Se 83,4%; Sp 76,4%; PPV 72,6%; NPV 76,8%; Colposcopy: Se 83,4%; Sp 69,4%; PPV 69,3 % ; NPV 80,6 %; After the excisional treatment: Pap :Se 82,8 %; Sp 92,3 %; PPV 61,5 %; NPV 97,3 %; Colposcopy :Se 62,1%; Sp 80,4 %; PPV 32,1 %; NPV 93,4%.

**CONCLUSION:** Sensitivity of Pap smear test before and after treatment is approximately equal. The sensitivity of colposcopy is higher before treatment 83,3% than after treatment 62,1%. After excisional treatment, the Pap smear test was considered to be a more sensitive test than colposcopy.

**INTRODUCTION**

In 2020, an estimated 604,000 new cases of cervical cancer were diagnosed globally(Sung et al., 2021). Standard cervical cancer screening procedures begin with Papanicolaou test (Pap test), if abnormalities are detected, colposcopy with biopsy performed. Cervical cancer can often be prevented through screening and treatment of precursor lesions. Diagnosis and management of cervical intraepithelial neoplasia (CIN) are critical steps in cancer prevention. High grade cervical intraepithelial neoplasia CIN2+ is a premalignant lesion that is diagnosed by histology CIN2 or grater, if left untreated, it can progress to cervical cancer-(World Health Organization, 2014) (Winer et al., 2005) (Mc Credie et al., 2008). Large loop electrosurgical excision (LEEP) of the transformation zone is most common treatment modality worldwide for cervical CIN2+ lesions. The manipulation allows removing the transformation zone with the minimal thermal damages of tissues(Sun et al., 2012) (Prendiville, 2009). Surgical treatment of high grade CIN with LEEP is safe procedure with low recurrence rates, resulting in a clearance of cervical HPV infection in the majority of cases (Duesing et al., 2012).

The Papanicolaou (Pap) test is most common screening method for detection of CIN and cervical cancer, and it has been effective in reducing the prevalence of this cancer and the associated mortality rates among woman. Despite of the huge success of the Pap test in cervical cancer prevention, several wide scale studies have shown high incidence of false negative results. Studies also suggested that 20% to 40% of new cervical cancer cases were diagnosed in those women, who had previously received screening, based on Pap test (Peirson Fitzpatrick-Lewis, D., Ciliska, D., Warren, R. ", Peirson, Fitzpatrick-Lewis, Ciliska, & Warren, 2013)(Subramaniam et al., 2011)(Leyden et al., 2005)(Kinney et al., 2014). Recent studies have evaluated accuracy of cytology ranging from 52% to 94% and accuracy of colposcopy to corresponding biopsy with outcomes ranging from a sensitivity of 70% to 98% and specificity 45% to 90% (Davies, Cantor, Cox, &

Follen, 2015). It should be noted that the treated women still remain under high risk of developing invasive cancer in comparison to the women of the general population of screening. This is determined by to the existence of residual/recurrent diseases following the treatment (van der Heijden, Lopes, Bryant, Bekkers, & Galaal, 2015). The risk of residual disease may vary from 5% to 30%. The majority of residual diseases are detected during 24 months post treatment (Kocken et al., 2011). There are some data, according to which the risk of persistent lesions exists during 10-20 years and likelihood of residual lesion is higher after the incomplete excision (Fuste et al., 2009)(Nuovo, Melnikow, Willan, & Chan, 2000)(Kocken et al., 2011)(Melnikow, McGahan, Sawaya, Ehlen, & Coldman, 2009).

In Georgian National Screening Center (GNSC) the treatment of precancerous conditions provided exclusively by LEEP. Suspicious on High Grade SIL based on the cytology (ASC-H, HSIL) and colposcopy GR2, or punch biopsy CIN2+ as well as persistence of CIN1 more than 2 years and/or CIN localization into cervical canal are considered as indication for LEEP procedures. The purpose of this study was to estimate the sensitivity, specificity, positive and negative predictive value of Pap smear test and colposcopy to identify cervical precancer before and after treatment of high-grade SIL (CIN2+). Aim of this study was to investigate the accuracy of Pap smear test and colposcopy to identify cervical precancer before and after treatment of high-grade SIL (CIN2+).

**Target Group And Research Methodology:**

The retrospective study included 613 patients diagnosed with cervical lesions who underwent excisional treatment of the cervix (LEEP) In the Georgian National Screening Center. The medical records from 613 women, were reviewed. In this group of patients, CIN2+ was observed in 285 woman. The definition of residual/recurrent disease during follow-up was biopsy proven CIN2 or worse, using punch or re -LEEP specimen. Women with at least two consecutive negative cytology smears and normal colposcopy findings after

treatment were considered negative for residual/recurrent lesion. In all cases conventional Pap smear test and colposcopy examination with or without biopsy was performed. The IFCPC 2011 nomenclature was used to grade colposcopic lesions. Colposcopic impressions were classified as normal, GR1 (low grade SIL), GR2 (high-grade SIL), or cancer. All LEEP specimens were evaluated by an experienced pathologist. The pathological report described the severity of disease, margin status and glandular involvement. The data were analyzed using SPSS version 21. By using descriptive indices, we determined the sensitivity, specificity, positive and negative predictive value of conventional Pap smear test and colposcopy. P value <0,05 considered to be statistically significant.

**RESULTS:**

The average age of the investigated women was 41 years (from 25 to 60 years).

Results of Histomorphological Examinations: 613 women in total, from them AIS-1 (0,2%), Carcinoma-12 (2,0%), CIN1-304 (49,6%), CIN2 -153 (25,0%), CIN3-119 (19%), negative for intraepithelial lesion 26 (4,2%) (table 1)

**Table 1. Distribution Of Patients According To Histopathology Results.**

Morphology	n	%
AIS	1	0,2
Carcinoma	12	2,0
CIN1	304	49,6
CIN2	153	25,0
CIN3	119	19
Negative	26	4,2
Total	613	100,0

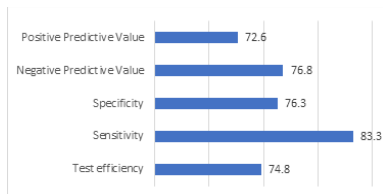
Using a disease threshold of HSIL sensitivity, specificity, positive and negative predictive value, of Pap smear test and colposcopy were analyzed before treatment (Table 2;3)(Chart 1;2)

**Table 2. Correlation Of Abnormal Pap Smear (asc/h/hsil) With Hystopathology (cin 2+) Before Leep**

Pap ASC-H/HSIL	CIN2+		Total
	Positive	Negative	
Positive	207	78	285
Negative	76	252	328
Total	283	330	613

p<0 001

**Chart 1 . Diagnostic value of Pap smear Cytology before LEEP**



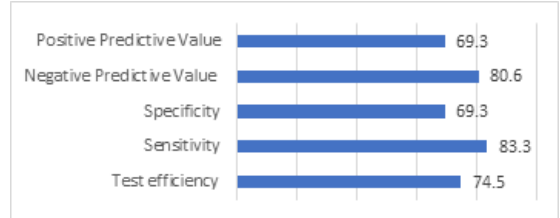
Sensitivity of Pap smear test : 83,3 % (95% CI 78,53%-87,53%), Specificity: 76,3 % (95% CI 72,40%-80,84%), PPV: 72,6 % (95% CI 68,34%-76,54%), NPV: 76,8 % (95% CI 73,05%-80,22%), Accuracy 74,8% (95% CI 71,25%-78,27%).

**Table 3. Correlation of abnormal Colposcopy (GR2) with hystomorphology (CIN 2+) before LEEP**

Colposcopy GR2	CIN2+		Total
	Positive	Negative	
Positive	228	101	329
Negative	55	229	284
Total	283	330	613

p<0 001

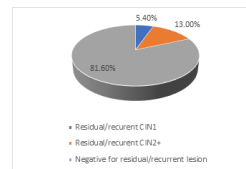
**Chart 2 .Diagnostic value of Colposcopy before LEEP**



Sensitivity of colposcopy: 83,3%(95% CI 78,53%-87,53%), Specificity: 69 3% (95% CI 64,11%-74,32%), PPV: 69,3 % (95% CI 65,52%-72,84%), NPV: 80,6 % (95% CI 76,47%-77,96%), Accuracy : 74,5 % (95% CI 70,91%-77,96%).

Follow-up observation after LEEP was carried out in 6, 12 and 24 months in 223 patients. During 2-year follow-up after LEEP, cytological abnormalities including ASC-H/HSIL were observed in 39 patients (17,4%), colposcopic abnormalities including ≥ GR1 were observed in 56 patients (25,1%). Forty one (18,4%) of 223 patients had residual/recurrent lesion during follow-up. Residual or recurrent lesions included CIN1 12 (5,4%) and CIN2+ 29 (13,0%). The research data were obtained by punch biopsy in 11 cases, and by repeated excisional treatment in 30 cases. The results of histomorphological examinations were distributed as follows (picture 1)

**Picture 1.**



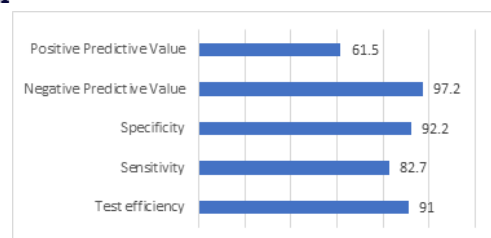
Using a disease threshold of HSIL sensitivity, specificity, positive and negative predictive value, of Pap smear test and colposcopy were analyzed after treatment for detecting the recurrent/residual disease. (Table 4;5)(Chart 3;4)

**Table 4. Correlation Of Abnormal Pap Smear (asc/h/hsil) With Hystopathology (cin 2+) After Leep**

PAP ASC-H/HSIL	CIN2+		Total
	Positive	Negative	
Positive	24	15	39
Negative	5	179	184
Total	29	194	223

p<0 001

**Chart 3 . Diagnostic value of Pap smear Cytology after LEEP**



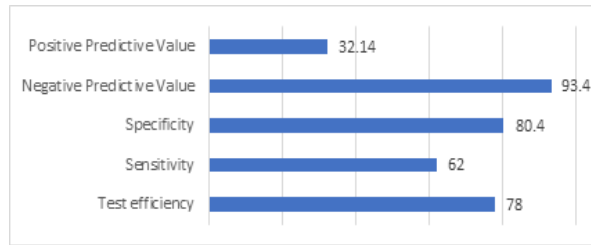
PAP smear Sensitivity : 82,7% (95% CI 64,23 %-99,15%), Specificity : 92,2 % (95% CI 87,57 %-95,61 %). PPV : 61,54 % (95% CI 48,41 %-72,78 %) NPV: 97,28 % (95% CI 94,16 %- 98,76%), Accuracy 91,0% (95% CI 86,49 %- 94,44 %).

**Table 5. Correlation of abnormal Colposcopy with Hystomorphology (CIN 2+) after LEEP**

Colposcopy GR1/GR2	CIN2+		Total
	Positive	Negative	
Positive	18	38	56
Negative	11	156	167
Total	29	194	223

p<0 001

**Chart 4 . Diagnostic Value Of Colposcopy After Leep**



Sensitivity of colposcopy: 62,0 % (95% CI 42,26 %-79,31 %); Specificity: 80,4 % (95% CI 74,12 %-85,75.%); PPV : 32,1 % (95% CI 24,05 %-41,47 %); NPV: 93,4 % (95% CI 89,86%-95,78%); Accuracy 78,0 % (95% CI 72,01%-83,28%).

**DISCUSSION**

Cervical cancer screening and treatment of precancerous lesions significantly reduces the risk of cervical cancer—(Smith et al., 2017). The risk of invasive cervical cancer among treated women is about five times greater than that among the general population, the possible reason for this may be poor long-term follow-up (Strander, Andersson-Ellström, Milsom, & Sparén, 2007) (Ghaem-Maghani, Sagi, Majeed, & Soutter, 2007). In most countries according to their national guidelines follow-up provided by Pap smear test and colposcopy (Anonymous, 2017). The role and value of colposcopy in follow-up has rarely been studied. Old studies present conflict results (Gardeil, Barry-Walsh, Prendiville, Clinch, & Turner, 1997)(Flannelly et al., 1997)——(Baldauf et al., 1998). According to those studies colposcopy does not significantly improve the sensitivity of cytology in early post-treatment follow up, while others report 100% sensitivity for colposcopy for residual disease. After treatment, epithelialization or scarring of the cervix might appear, making assessment of the transformation zone unreliable. The likelihood of detecting histological HSIL is much greater when performing colposcopy for HPV-positive women after treatment, whereas adverse effects are likely to dominate if colposcopy is routinely performed for all women during follow-up (Heinonen et al., 2020).

According to our research, the CIN lesion following the excisional treatment, was reported in 18.4% of patients in total (CIN2 + 13.0%, CIN1 5.4%), while if we consider CIN2+ dysplasia, defined by histomorphological research, as the true residual lesion, then the percentage rate of residual disease is 13,0%. The CIN1 lesion following the treatment may be the result of repeated HPV infection rather than the residual lesion, although it is noteworthy that often low grade and high grade dysplasia is combined in one lesion (Park et al., 2009)(Giannella et al., 2015). This finding is similar to the reported incidence in previous studies. (Alonso et al., 2006)(Lubrano et al., 2012)(Zappacosta et al., 2013). Such number of residual lesions then again underlines the necessity of the follow-up.

Currently, the Pap test and colposcopy are provided as diagnostic tests within the Georgian national screening program. According to our study sensitivity of Pap smear cytology before and after treatment is nearly similar (83,4 % vs 82,8 %), sensitivity of colposcopy is much more higher before treatment 83,3% than after treatment 62,1%. The low-sensitivity of the colposcopic examinations in the treated women may be determined from the one hand by the fact that, after the treatment in frequent cases is observed the transformation zone type III, (SCJ is not visualized, the lesion is localized in the cervical canal) while on the other hand the immature squamous metaplastic epithelium, which often leads to imitation of CIN. Sensitivity of Pap smear test is higher than Sensitivity of colposcopy in treated (post LEEP) patients 82,8 % vs 62.1%. Our results are within the range of other estimates in the literature (Davies et al., 2015) (Ghosh et al., 2014). Data outcomes of our study reveals the similarities with

results of other European studies and they could be considered as The National parameters for Georgia.

**Abbreviations:**

- SIL-Squamous Intraepithelial Lesion;
- CIN2+ Cervical Intraepithelial Neoplasia grade 2 or greater
- LEEP - Loop Electrosurgical Excision Procedure
- HSIL-High grade Squamous Intraepithelial Lesion
- Se-Sensitivity
- Sp-Specificity
- PPV, NPV – Positive and Negative Predictive Values

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