# CORRELATION BETWEEN COLPOSCOPIC IMPRESSION AND HISTOLOGIC DIAGNOSIS OF PREMALIGNANT LESIONS OF THE CERVIX

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## Abstract

***Background:*** Cervical cancer is the commonest cancer in sub-Saharan African with majority of the women presenting with an advanced disease stage. This is largely due to the unavailability of an established cervical cancer screening programme in most countries. This also includes the use of colposcopy which is still not available to many gynaecologists practicing in Nigeria.

***Aim:*** To review reports of colposcopy carried out at the University of Abuja Teaching Hospital, Abuja, Nigeria and to determine the degree of concurrence between colposcopic impression and histologic diagnosis.

***Methods:*** A retrospective analysis of the colposcopic findings of 84 patients was done. Subsequent correlation with histopathology report was carried out in 53 patients who had colposcopically directed biopsies between March 2012 and February 2014.

***Results:*** The commonest impression made on colposcopy was high grade CIN in 40(47.6%) patients. The concurrence rate between colposcopic findings and histology diagnosis was 64.2% (34/53) {K =0.302, 95%CI= -0.010-0.436}. The concurrence rate was higher for high grade CIN 29/40(72.5%) than for low grade CIN 5/12 (41.7 %). There was an overestimation of colposcopic diagnosis in 13(24.5%) patients and an underestimation in 6(11.3%) patients. The sensitivity of colposcopy for detecting high grade lesions or more was 32/36(88.9%) while the specificity was 8/17(47.1%). False positive rate for high grade lesions was 9/17(52.9%) and false negative rates for low grade lesions was 4/36(11.1%). Positive predictive value (PPV) of high grade colposcopic diagnosis or more was 32/41(78.04%) while the negative predictive value (NPV) was 8/12(66.73%).

***Conclusion:*** The strength of agreement between colposcopic diagnosis and cervical pathology was fair and colposcopy performs better in the detection of high grade lesions.

***Key Words:*** *Cervical cancer, Premalignant lesions, Colposcopy, Histopathology, Nigeria*

## Introduction

Cervical cancer is the second most common cause of cancer related morbidity and mortality in developing countries and this disparity has been attributed to a reduction in the incidence of invasive cancer in developed countries following implementation of

It has been established that premalignant and malignant diseases of the cervix evolve very slowly, over a significant time frame and it is for this reason that cervical cancer has been said to be preventable and curable especially when there is early detection and effective treatment of these lesions [4]. Methods for early detection of pre-invasive lesions of the cervix include the Papanicolaou (Pap) smear, HPV DNA testing, visual inspection with acetic acid (VIA) and visual inspection with Lugols's iodine (VILI). Colposcopy on the other hand is used for verification of the reports of all these screening procedures[5].

The Pap smear is usually employed in resource rich settings due to affordability of resources required and availability of expertise. The latter two which are visual screening methods require fewer resources and expertise and as such, are being advocated for use in resource poor settings[6].

As far back as the early 70's, treatment for abnormal pap smear results was a cone biopsy and specimen obtained were then examined. The histology results however revealed a significant number of false positives. This tendency for overtreatment became a source of concern especially with regard to the cost of treatment and complications associated with cone biopsy and subsequently led to a quick introduction of colposcopy as a method of screening and identifying women who have abnormal results and truly need treatment for their disease[7]. Its use has also led to the reduction in unnecessary cone biopsies as a result of its ability to delineate lesions, thereby making them more amenable to other forms of conservative therapy[8, 9, 10]. This indispensable facility unfortunately is available only in a few tertiary institutions like ours.

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The outcome of colposcopy depends on the experience of the colposcopists and this has led to scrutiny of the ability of the colposcopist to determine accurately the severity of intraepithelial lesions and even to diagnose early invasion[11, 12]. Some older studies showed a low perfect agreement between the colposcopic impression and histologic diagnosis within the range of 32% −37%, with a weighted kappa strength of agreement of only 0.20-0.26 while the agreement within one grade was reported to be only 75% −77% [10, 13]. Reports of more recent studies however have shown some improvement with perfect agreement rates of 57-65% and agreement within one grade being reported to be as high as 94-98%[14, 15, 16]. These differences in reported rates of agreement by various studies has made the subject of optimization of accuracy of colposcopy and biopsy specimen in the detection of premalignant lesions one of the leading concerns in the entire cervical screening process. One of the efforts made in achieving this is the development and publication of a new system of terminology by the International Federation for Cervical Pathology and Colposcopy (IFCPC) in 2011[17]. Adoption of this system by most researchers is likely to go a long way in providing uniformity in reporting colposcopy findings and by so doing, provide justification for comparison of results.

In addition to unavailability of equipment, other challenges encountered in the management of women with cervical pathology in low resource settings like ours border on ignorance, accessibility and cost. A study done in southeastern Nigeria reported a high rate of refusal of colposcopy and with only few institutions in Nigeria offering colposcopic services, many women having to travel long distances to access this service[18]. This and also their inability to meet the expenses subsequently leads to a high rate of loss of patient to follow up. There is therefore an urgent need to educate the women on the importance of colposcopy and the need to make the service more accessible and more affordable.

Conservative surgical management of cervical intraepithelial neoplasia include excisional or ablative procedures. Excisional procedures comprise of laser conization, cold-knife conization, and electrosurgical loop excision (Loop Electrosurgical Excision Procedure). The excisional method is preferred since its allows for histological diagnosis and provides treatment at the first visit. Cure rates of more than 90% have been recorded after one treatment[2, 19]. Consequently, the "see and treat" approach in which loop excision is performed at initial colposcopy is an acceptable option for high-risk, adult patients who present with high-grade cytology and corresponding colposcopic abnormalities. A prospective study using this approach found that 84 percent of patients had cervical intraepithelial lesion (CIN) 2 or 3 within the excisional biopsy specimen[19].

Due to availability of the colposcope in the University of Abuja Teaching Hospital (UATH), Abuja, Nigeria, this study set out to review reports of colposcopy, determine the degree of concurrence between colposcopic impression and histologic diagnosis and evaluate the positive predictive value (PPV) and the negative predictive value (NPV) of the high grade lesions on colposcopy.

## Methodology

### *Study design*

A two-year retrospective study of patients seen in the colposcopy clinic of the University of Abuja Teaching hospital (UATH), Abuja between 1st March 2012 to 28th Feb 2014. The list was obtained from the register in the colposcopy clinic and subsequently used to retrieve the patient's folders so as to obtain relevant information. Data obtained with the aid of a structured proformas include: age, parity, indications for colposcopy/pap smear reports, colposcopy reports, histology reports of biopsy specimen and treatment offered.

### *Study Area/ Protocol*

Colposcopy in UATH is performed every Monday and Wednesday by two consultant gynaecologists trained to perform colposcopy. It is done on an out-patient basis, following the standard procedure with 5% acetic acid. Multiple colposcopically directed biopsies are taken from suspicious lesions using the punch biopsy forceps. Biopsy fragments are processed and read in the Pathology Laboratory of the UATH. The colposcopic findings and histological diagnosis were reported as normal, benign, low grade lesion, high grade lesion, microinvasive cancer (MIC) and invasive cancer. Patients whose histology reports confirmed high grade lesions were treated with loop electrosurgical excision procedure (LEEP) or cryotherapy. Patients whose histology confirmed invasive cancer were managed as per standard protocol.

### *Data analyses*

This was done with the aid of Statistical Package for the Social Sciences (SPSS) version 20. Categorical variables were represented as percentages while continuous variables were reported as mean and standard deviation. The agreement between colposcopic diagnosis and cervical pathology was determined using weighted Kappa statistics. Sensitivity, specificity, PPV, NPV, false positive rate and false negative rate were used to compare colposcopic diagnosis and cervical pathology.

## Results

There were 106 women seen over the period of 2 years however only 84 folders could be retrieved for analysis. This gave a retrieval rate of 79%. Biopsies were not taken from the non-malignant category for histologic examination. The mean age of the patients was 41.7 ± 9.9years (Range 22-66 years).

Table 1 shows the age and parity distribution of the patients. The age group with the highest number of women 30(35.7%) was the 40-49year group while the least number, 8(9.5%) were in the 20-29year group.

Most of the patients were multiparous, with only 12(14.3%) of them being nulliparous.

**Table 1:** Age and Parity distribution of patients.

| Age | n=84 | Percentage (%) |
|---|---|---|
| **Age group** | | |
| <20 | 0 | 0.0 |
| 20-29 | 8 | 9.5 |
| 30-39 | 27 | 32.1 |
| 40-49 | 30 | 35.7 |
| >49 | 19 | 22.6 |
| **Parity** | | |
| 0 | 12 | 14.3 |
| 1-4 | 50 | 59.5 |
| **≥5** | 22 | 26.2 |

The most common indication for colposcopy was an abnormal pap smear which was either a persistent low grade squamous intraepithelial lesions (LGSIL) in 20(23.8%) of cases or high grade squamous intraepithelial lesions (HGSIL) in another 20(23.8%). The least common indications were adenocarcinoma in-situ (AIS) and atypical squamous cells of undetermined significance (ASCUS) on cytology, seen in 1(1.2%) patient each (Table 2).

**Table 2:** Indications for colposcopy.

| Pap smear report | Frequency | Percent (%) |
|---|---|---|
| Persistent inflammatory changes on cytology | 11 | 13.0 |
| ASCUS on cytology | 1 | 1.2 |
| AGC on cytology | 2 | 2.4 |
| AIS on cytology | 1 | 1.2 |
| Persistent LGSIL on cytology | 20 | 23.8 |
| HGSIL on cytology | 20 | 23.8 |
| Invasive cancer on cytology | 3 | 3.6 |
| Persistent unsatisfactory quality on cytology | 5 | 6.0 |
| Post coital bleeding | 3 | 3.6 |
| Suspicious cervix | 18 | 21.4 |
| **Total** | **84** | **100** |

HPV: Human Papillomavirus, ASCUS: Atypical squamous cells of undetermined significance, AGC: Atypical glandular cells, AIS: Adenocarcinoma insitu, LGSIL: Low grade squamous intraepithelial lesion, HGSIL: High grade squamous intraepithelial lesion.

Table 3 illustrates the frequency of various colposcopic impressions of the patients.

The commonest impression made was high grade CIN, seen in
40(47.6%) of patients while the least impression made was micro-invasive cancer, seen in 1(1.2%) patient. An impression of low grade CIN was made in 12(14.3%) of patients.

**Table 3**: Colposcopic impressions of the patients

| Findings | Frequency (n) | Percentage (%) |
|---|---|---|
| Normal | 17 | 20.2 |
| Benign | 14 | 16.7 |
| Low grade CIN | 12 | 14.3 |
| High grade CIN | 40 | 47.6 |
| MIC/Invasive cancer | 1 | 1.2 |
| Total | 84 | 100 |

CIN-Cervical intraepithelial neoplasia, MIC-microinvasive cancer

Table 4 shows the age distribution of patients with premalignant and micro-invasive/invasive lesions on colposcopy. Sixteen (40%) patients with high grade lesions were within the 30-49year age group while 6(50%) of patients with low grade lesions were in the age group 40-49 years. The only patient with micro-invasive disease was also in the 30-39year age group. Analysis of parity distribution shows that nulliparous women had the lowest frequency of premalignant lesions 6(11.3%) while women with parity between 1-4 had the highest frequency, 32(60.4%) (Table 5).

**A**greement between colposcopic impression and cervical biopsy pathologic diagnosis is shown in table 6. The percentage (%) concurrence between colposcopic findings and histologic diagnosis was 64.2% (34/53) {K =0.302, 95%CI= -0.010-0.436}. The concurrence rate was higher for high grade CIN 29/40(72.5%) than low grade CIN 5/12(41.7 %.). There was an overestimation of colposcopic diagnosis in 13 patients (24.5%) and an underestimation in 6 patients (11.3%).

Table 7 shows agreement between colposcopic impression and histologic diagnosis of cervical biopsy specimen for low grade and high grade lesions. The sensitivity of colposcopy for detecting high grade lesions or more is 32/36(88.9%) while the specificity is 8/17(47.1%). False positive rate for high grade lesions is 9/17(52.9%) and false negative rates for low grade lesions is 4/36(11.1%). Positive predictive value (PPV) of high grade colposcopic diagnosis or more was 32/41(78.04%) while the negative predictive value (NPV) was 8/12(66.73%).

Concerning treatment modalities offered to patients, majority of the patients, 29(61.7%) had loop electrosurgical excision procedure (LEEP), 13 (27.7%) had hysterectomy and 4(8.5%) had cryotherapy. One of the patients with invasive cervical cancer on histology was referred, based on request for further management (Not shown in table).

**Table 4:** Age distribution of patients with premalignant and microinvasive/invasive lesions on colposcopy.

| Age(years) | Low grade lesion | High grade lesion | MIC/Invasive cancer | Total |
|---|---|---|---|---|
| **<20** | 0 | 0 | 0 | 0 |
| **20-29** | 0 | 3 | 0 | 3 |
| **30-39** | 4 | 16 | 1 | 21 |
| **40-49** | 6 | 11 | 0 | 17 |
| **>49** | 2 | 10 | 0 | 12 |
| **Total** | **12** | **40** | **1** | **53** |

**Table 5:** Parity distribution of patients with premalignant and microinvasive/invasive lesions on colposcopy.

| Parity | Low grade CIN | High grade CIN | MIC/Invasive cancer | Total (%) |
|---|---|---|---|---|
| **0** | 3 | 3 | 0 | 6 (11.3) |
| **1-4** | 8 | 23 | 1 | 32 (60.4) |
| **≥5** | 1 | 14 | 0 | 15 (28.3) |
| **Total** | 12 | 40 | 1 | 53 (100) |

**Table 6.** Comparison of Colposcopic Impression and Histologic Diagnosis

| Colposcopic Diagnosis | Cervical biopsy Pathology | | | | |
|---|---|---|---|---|---|
| | ***Normal/Benign*** | ***CINI*** | ***CINII/III*** | ***Microinvasive/Invasive cancer*** | **Total** |
| *Benign* | 0 | 0 | 0 | 0 | 0 |
| *CINI* | 3 | 5* | 4 | 0 | 12 |
| *CINII/III* | 0 | 9 | 29* | 2 | 40 |
| *Invasive cancer* | 0 | 0 | 1 | 0 | 1 |
| *Total* | 3 | 14 | 34 | 2 | 53 |

*Concurrence

**Table 7.** Agreement between Colposcopic Impression and Histologic Diagnosis of Low Grade and High Grade Lesions

| Colposcopic Diagnosis | Cervical biopsy pathology | | |
|---|---|---|---|
| | **Normal/Benign/CINI** | ***CINII/III* /Cancer** | **Total** |
| Normal/Benign/LGSIL | 8 | 4 | 12 |
| HGSIL/Cancer | 9 | 32 | 41 |
| Total | 17 | 36 | 53 |

## Discussion

Early detection can prevent death from cervical cancer, but success is dependent on women with abnormal cytology attending follow-up procedures, including colposcopy. Since there are no organized screening programs in Nigeria, opportunistic cervical cancer screening with Pap smear is offered to women attending the gynaecological clinic of the University of Abuja Teaching Hospital (UATH), with subsequent referral for colposcopy within the hospital when indicated. Most of the patients seen were within the 30-49year age group and were also multiparous.

There were several indications for this examination and an abnormal Pap smear test is usually the most frequent indication for colposcopy followed by a suspicious looking cervix [4, 20]. This was the finding in this study where 69% were referred for colposcopy due to an abnormal cervical cytology. Women with a low grade lesion can be followed up with cytology in 6 months and those with persistent or progressive disease are referred for colposcopy [2, 18]. This is what is practiced in UATH. However, in centres with facilities for HPV DNA test, co testing could be carried out and those with a positive high risk HPV test are referred for colposcopy. A study done by Cecchini et al [21] suggested that screening by colposcopy when compared to conventional cytology screening is more sensitive and therefore maybe more feasible and cost effective on the long run. However, the major drawback of primary colposcopy is its low specificity with the consequence of false-positive rate and over-treatment in a substantial number of cases [22].

In this study the perfect agreement between colposcopic impression and histologic diagnosis was 64.2%. This result is lower than reports by Mousavi et al.[23] and Durdi et al.[24] but similar to the findings by Li

et al.[15] and Fan et al.[16] even though the strength of agreement in their study was moderate at a Kappa value of 0.436-0.494 while ours was fair at 0.302. It is important to note that these similar results were obtained despite use of different criteria in reporting the colposcopic findings. Take for instance, Fan et al.[16] and Li et al.[15] used the 2011 IFCPC criteria but in our study, diagnosis was based on identification of well-defined characteristics or use of the Reids Colposcopic index (RCI) [25], depending on the consultants preference. Mousavi et al.[23] and Durdi et al.[24] had employed the use of Reids Colposcopic index (RCI). Although this maybe a drawback in the comparison of the results of the various researches, results obtained seem to explain why there is still some controversy surrounding the use of any one set criteria in the practice of colposcopy. It is possible that the skill and experience of the colposcopist may be more significant than the application of a set of criteria, an example can be seen in the study done by Massad et al.[10] where colposcopy carried out by resident doctors reported a much lower perfect agreement rate of 37%.

Non correlation between colposcopy and histology could result from colposcopic findings not apparent to the examiner, visualized lesions not included in biopsy specimens, lesions not included in the sections of paraffin embedded tissue or the pathologists inability to identify the lesion within the submitted specimens. Multiple biopsies have been said to increase colposcopy and histology correlation [4,13]. Training and retraining of colposcopists with constant practice to maintain proficiency should therefore be encouraged as there is still great inter-observer differences with colposcopic diagnosis especially low grade CIN even among expert colposcopists.

In our study, colposcopy recorded a higher frequency of overestimate (24.5%) compared to underestimate (11.3%) and this was reflected by a high rate of false positive reports of high grade lesions (52.9%). Overestimation in colposcopy leads to overtreatment while underestimation has the danger of failure to identify patients at risk therefore, with this understanding, it is imperative that the practice of colposcopy be done in line with best practices so as to ensure accuracy of results.

Studies have revealed that the positive predictive value of colposcopy is better with an increase in the severity of the cervical lesion and considerably so when biopsies are taken. However, the positive predictive rate for microinvasive disease is poor probably due to the absence of characteristic features [4]. This was seen in this study in which there was a 100% downgrade for microinvasive disease. In our study also, the sensitivity for diagnosing high grade or higher lesions by colposcopy was 88.9% and this performance is higher than 56% reported by Massad et al.[10] but similar to 64-71% reported by Li et al. [15] and Fan et al. [16]. The specificity of the high grade lesions in our study (47.1%) was however lower than values reported these researchers [15, 16] who got values as high as 98% and 97% respectively. These authors had used the 2011 IFCPC terminology and this evidence seems to support the argument for the need for application of this terminology in ruling out high grade disease. It is also important in terms of subsequent patient management as it helps to prevent over treatment.

Our study found a similar PPV for HGSIL+ (78%) when compared to other studies [14, 15, 16]. However, the negative predictive value for these high grade lesions was 66.1% and this was lower than the value reported by Li et al.[15] and Durdi et al.[24]. Since the focus of the entire process therefore is detection and treatment of high-grade disease with the aim of reducing the incidence of cervical cancer, we therefore recommend that going forward, a more structured approach to colposcopy be employed as the practice of colposcopy increases in our environment.

This study also noted that with the increase in the practice of colposcopy, especially in tertiary centers like ours, conservative management approaches are also increasing as evidenced by 61.7% of patients who were managed with the loop electrosurgical procedure. Overall however, a systematic review on cervical cancer prevention and treatment in Africa has shown that challenges are still significant in low resource settings in terms of availability of infrastructure, expertise, cost and patient compliance [26].

The limitations of this study include its retrospective nature and the non-use of a single and definite criteria which may make colposcopic assessment more subjective.

## Conclusion

In conclusion, the strength of agreement between colposcopic diagnosis and cervical pathology was fair and colposcopy performs better in the detection of high grade lesions. More research aimed at assessing the practice and improving the diagnostic accuracy of colposcopy is needed in our environment.

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## Conflicts of Interest

There are no conflicts of interest

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