ORIGINAL ARTICLE

Colposcopy: A Valuable Screening Tool for the Diagnosis of Premalignant and Malignant Cervical Pathologies

Attiqa Zaigham, Asma Shaheen, Azra Saeed Awan, Raazia Rauf

ABSTRACT

Objective:To correlate colposcopic findings with the results of cervical biopsy and to prove colposcopy as a valuable screening tool for the diagnosis of premalignant and malignant cervical pathologies.

Study Design: A quasi experimental study

Place and Duration of Study: Study was conducted from January 2008 to April 2010 in the Department of Obstetrics & Gynecology, Railway Hospital Rawalpindi.

Materials and Methods: The study population included three hundred women who attended the outpatient department of Railway hospital over a period of two years. All these symptomatic women between the ages of 30-60 years were recruited with one or more of the complaints of post coital bleeding, intermenstral bleeding, postmenopausal bleeding, recurrent vaginal discharge or abnormal Pap smear.

The recruited women were examined by speculum, followed by pap-smears. Out of 300 women Pap smear of 200 women was abnormal and showed inflammatory lesions at three consecutive times. These ladies were booked for colposcopy. However, any other women whose reports showed dyskaryotic changes were immediately booked for colposcopy. Biopsies from abnormal areas were taken and sent for histopathology. The reports of cervical biopsy were then analyzed.

Results: Out of 300 women recruited, 200 showed positive Pap smear. 108(54%) symptomatic women showed normal epithelium, while 92 women (46%) had abnormal transformation zone changes. Cervical biopsy reports of 92 women with abnormal colposcopic findings, showed up chronic cervicites in 60 cases, miscellaneous cervical pathologies in 10 cases, no dysplasia in 10 cases and cervical carcinoma was diagnosed in 12 cases.

Conclusion: The study concluded that colposcopy followed by cervical biopsy proved to be a valuable screening tool for the diagnosis of premalignant and malignant cervical pathologies.

Keywords: *Colposcopy, Dysplasia, Cervicitis, Cervical carcinoma.*

Introduction

Benign diseases of the cervix are common, usually asymptomatic or cause minor symptoms. However they must be differentiated from malignancy. Cervical cancer is the second commonest cancer among women in developing countries; with an estimated lifetime risk of 0.1865 %.[1] It is preceded by a premalignant form years before its invasion. Therefore, screening for premalignant disease of the cervix can markedly reduce the morbidity and mortality from cervical cancer.[1] Screening with Papanicolaou (Pap) smears, followed by colposcopy with biopsy for diagnosis and LETZ excision for treatment has become the standard of care for developed countries due to its effectiveness in reducing the population-wide incidence of invasive cervical cancer and its overall cost-effectiveness.[2]

Pakistan is among the poorest country in the Southeast Asia; two-thirds of the Population lives below the poverty line and half of them lack basic sanitation and portable water. The cervical cancer incidence in Pakistan is 39.1/100,000 (.0391%).[3] These rates are over four times higher than in the United States[4] The healthcare resources are scarce in our country and there are limited screening programs available. Moreover lack of awareness among women, social taboos, social limitations and immobility, all

Coresspondence:
Dr Attiqa Zaigham
Senior Registrar
Dept of Gynae/Obs
Pakistan Railway Hospital
IIMCT, Rawalpindi

provide barriers to early detection of cancer. Pakistan has no nationwide cervical cancer screening program, but Pap smears are widely available through local health centers, at private clinics, or at special screening days organized by a variety of private organizations. Even doing Pap smear has many limitations as many clinics lack spatulas, cytobrushes, and fixative and instead used tongue depressors, Q-tips, and hair spray. In few settings specimen are often stored in warm, humid conditions for one or more weeks prior to transport to the central processing facility, resulting in fungal contamination. Most of our central laboratories lack the resources to purchase new supplies on a regular basis, so dyes and stains were re-used and recycled to extend their use, resulting in poor quality staining. Therefore in such settings relying only on Pap-smear can be questionable.

Colposcopy, a clinical method of proved accuracy, in such settings can be an excellent means of evaluating abnormal cervical cytology. During colposcopy, Visual Inspection with Acetic Acid (VIA) coupled with Pap smear reports can provide an effective screening tool in developing countries like Pakistan. Colposcopy is available only at a limited number of Government Hospitals. However the attractive features of colposcopy include immediate availability of results, and accuracy comparable to that of good quality Pap smears. Fortunately, colposcopic examination is satisfactory not in older women but quite accurate in nearly all young patients who mostly need conservative treatment.[5]

The rationale of our study comes from the need for early detection to decrease the incidence of cervical Cancer in Pakistan as we all are well aware that there are usually years between dyskaryotic changes, CIN and invasive carcinoma.

Materials and Methods

A quasi experimental study was conducted from January 2008 to April 2010 in the Department of Obstetrics & Gynecology, Railway Hospital Rawalpindi.

The study population included total of three hundred women who attended the outpatient department of Railway hospital over a period of two years. In study, during initial evaluation of women we first explored different variables like the age at first intercourse, HPV infection, STDs, multiparty, history of previous CIN, smoking, immunocompromised state and poor personal hygiene. All the data recorded on a specially designed Performa.

Out of these two symptomatic women between the ages of 30-60 years, smoker or non smoker, with any or more of the complaints of recurrent abnormal vaginal discharge, erosion/ ectropion on cervix, an unhealthy cervix or any cervical lesion which is bleeding on touch, previous abnormal Pap smear, post coital bleeding, intermenstral bleeding, and postmenopausal bleeding were recruited. Pregnant women, women with uterovaginal prolapsed;Post hysterectomy and post radiation cases were excluded.

The recruited women were examined by speculum, followed by pap-smears. The prepared Pap smear slides were sent for cytological examination in our hospital. Smears were reported either as Normal, Unsatisfactory/insignificant changes, Inflammatory or borderline. All borderline cases group included cases showing mild, moderate, or severe dyskaryosis or showing abnormal glandular cells. These ladies were immediately recruited for suspicion of malignancy and booked for colposcopy.

16

All other women whose cytological reports showed inflammatory response were first treated by antibiotics for fourteen days and then their Pap-smears repeated. Out of this group, all those women who's Pap smear still showed inflammatory lesions at three consecutive times were also booked for colposcopy.

During colposcopy all women underwent both acetic acid and Schiller's test. The colposcopic findings and suspicious biopsy sites were recorded on specially designed Performas and their colposcopic picture was drawn accordingly. The acetowhoite areas and iodine negative areas were selected sites for cervical biopsies. Interpretation of colposcopy reports were on finding acetowhite leisions, surface pattern of lesion, vascular/mosaic pattern or whether it was a single, bifocal or annular leisions. All these findings were then interpreted according to Clinicocolposcopic index. Maximum score was set as 10, 0-2 was for insignificant lesion, 3-5 for low grade lesion and 6-10 for high grade lesion (Table I).

Women with abnormal colposcopic findings were admitted for cervical biopsy, biopsies taken and sent for histopathology. The reports of cervical biopsy were then analyzed and work up planned accordingly. The histopathological cervical biopsy findings were categorized according to the nomenclature into:

*Normal,*Abnormal,*Undifferentiated and *Miscellaneous.

Normal included all those: when there was no cellular evidence of neoplasia whether or not there were organisms such as Trichomonas vaginalis or Fungal organisms morphologically consistent with Candida spp or Shift in flora suggestive of bacterial vaginosi or Cellular changes consistent with Herpes simplex virus.

Abnormal cases included: Cases showing either Atypical squamous cells of undetermined significance (ASC-US), Low grade squamous intraepithelial lesion (LSIL) (encompassing: HPV/mild dysplasia/CIN 1), High grade squamous intraepithelial lesion (HSIL) (encompassing: moderate and severe dysplasia, CIS, CIN 2 and CIN 3) with features suspicious for invasion (if invasion is suspected) or Squamouscell carcinoma.

Miscellaneous group included cases of Nabothian cyst, reactive changes due to IUCDs, radiation, post hysterectomy or atrophy.

All the study variables including Pap smear reports, colposcopy findings, histopathological diagnosis, age of the patient, parity, smoking and history of previous cervical malignancies were calculated. The data was entered and confidence interval calculated.

Table I: Clinicocolposcopic Index

	0	1	2
Index cytology	Low grade		High grade
Smoking	No		Yes
Age(years)	< 30		>30
Acetowhitening	Slight		Marked
Surface area(cm2)	<1	>1	
Intercapillary distance(µm)	<350 no mosaic punctation	>350 mosaic punctation	
Focality of lesion	Unifocal or multifocal	Annular	
Surface pattern	Smooth	Irregular	

Results

Out of 300 women recruited, 200 showed positive Pap smear. Out of these 200 patients, 96 (32%) were in the age group of 30-39 years, 57(19%) were 40-49 years and 147(49%) were in the age group of 50-59. One hundred and seventeen (39%) were in the parity group 0-4 and 183 (61%) were in the parity group 4-6.The major presenting

17

complaints were a white discharge per vaginum and lower abdominal pain. Most of the patients with dysplasia had white discharge per vaginum and post-coital bleeding.

Out of 200 patients with positive Papanicolaou smears, 108(54%) women showed normal epithelium at colposcopy, while 92(46%) had abnormal transformation zone changes. In 108 women, colposcopic directed biopsy evaluation was not done because we would have expected the biopsy specimens to be negative as they had no significant findings at colposcopic examinations.

Out of 200 positive cases, Pap smear reports picked 4 cases with dyskaryotic changes. All these positive cases were examined under colposcope and underwent cervical biopsy. 92(46%) of these women had showed abnormal epithelium changes and underwent cervical Biopsy. The abnormal findings on colposcopy were acetowhoite areas, punctation, mosaic pattern and an abnormal vasculature or nabothian cyst (Figure 1).

In 92 women with abnormal colposcopic

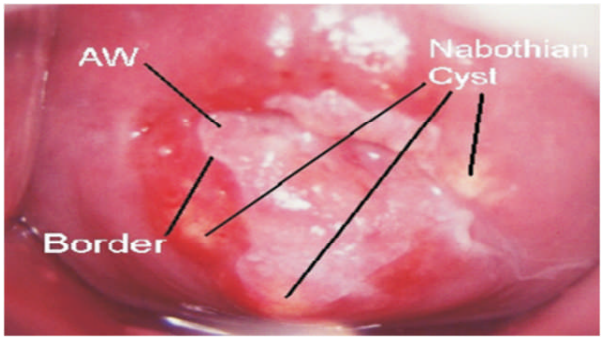

Figure 1: Colposcopic picture showing acetowhoite areas, an abnormal vasculature as punctation and nabothian cyst.

findings, the cervical biopsy revealed that sixty cases had chronics cervicites, ten cases were of miscellaneous cervical pathology, ten cases showed no dysplasia and cervical carcinoma was diagnosed in twelve cases. Out of these twelve cases, 5 women showed Low grade squamous intraepithelial leisions, 2 had High grade intraepithelial leisions and 5 with invasive leisions were picked. Using the same data, we calculated the percentage of positive and suspicious tests and their confidence interval calculated (Table II).

Cervical biopsy reports of 4 cases with

Table II: Results of Colposcopically directed biopsies for patients with positive Papanicolaou smear and suspicious colposcopy

Tissue diagnosis	Positive Pap smear Suspicious colposcopy	Prevalence	Confidence index
Chronic cervicites	60	60/92	65.21%
Miscellaneous cervical pathologies	10	10/92	10.86%
No dysplasia	10	10/92	10.86%
CIN 1	5	5/92	5 43%
CIN 2	2	2/92	2 17%
CIN 3	5	5/92	5.43%
Total no of CIN lesions	12	12/92	13.04%
Total	92		

dyskaryotic changes on Pap smear and suspicious colposcopy were also diagnosed to have CIN I & 3.Cervical biopsy reports of 8 cases with both Pap smear and colposcopy showed CIN 1, 2 & 3. Total twelve patients with cervical intraepithelial neoplasia lesions were detected by using both methods followed by colposcopically directed cervical biopsies (Table III)

Further Analysis of the result showed that

Table III: Colposcopically directed biopsies for patients with either positive Papanicolaou smear or Pap smear plus colposcopy

Tissue diagnosis	Pap smear	Colposcopy	No. of patients
No dysplasia	-	10	10
CIN 1	3	2	5
CIN 2	0	2	2
CIN 3	1	4	5
Total	4	18	22
Total no. of CIN lesions	4	8	1 2

18

screening of 200 women by both the Papanicolaou smear and colposcopic examination and subsequent biopsies was more effective than Pap smear alone. In these women, the screening alone with Pap smear picked up only 4/92(4.35%) cases (table 4). Pap smear alone failed to diagnose abnormalities in 88 cases, which were diagnosed colposcopically and histologically.Pap smear when coupled with colposcopic evaluation and the guided biopsy were successful in detecting abnormalities in 92 cases. Colposcopy picked up 8/92(8.7%) cases. Colposcopy proved to be more sensitive when coupled with the Papanicolaou smear as it helped in detection of other cervical pathologies also and cervical intraepithelial neoplasia. The incidence of CIN 1 and CIN 2, 3 was found to be 5.43 % and 7.60 % respectively in the present study.The sensitivity and the specificity of colposcopy& Pap smear to diagnose premalignant and malignant leisions were 75% and 50% respectively. The predictive value of colposcopy in the present study was 42.85% (Table IV)

The sensitivity of colposcopy when coupled with Pap smear to diagnose premalignant and malignant leisions decreased from 75% to 58.33% but the specificity of colposcopy& Pap smear improved from 50% to 57.44% respectively.

Table IV: Papanicolaou smear alone & papsmear coupled with Colposcopy

	Positive Pap smear	Colposcopy & Positive Pap smear	Total
Premalignant Leisions	3	4	7
Malignant	1	4	5
Total	4	8	12

Depending upon their degree of dysplasia, the young patients with mild dysplasia were subjected to conservative treatments like cryotherapy and conization. The perimenopausal and post menopausal women were booked for surgery.

Discussion

The worldwide burden of cervical disease is enormous, with over 500 000 new cases of cervical cancer diagnosed each year, resulting in 250 000 deaths. This burden and ramification of cervical cancer due to Human Papilloma virus (HPV) infection is significantly and proportionally greater with over 300 million new cases of HPV infection, 30 million new cases of Low Grade Squamous Intraepithelial Lesions (LSIL) and 10 million new cases of high-grade squamous intraepithelial lesions (HSIL) diagnosed yearly.[6]

The prevalence of cervical disease is highest in underdeveloped countries and lowest in developed countries where screening program's have significantly reduced the incidence of disease.[7] Cervical cancer mortality in the Netherlands has been steadily declining in the last decades, largely as a result of a well-functioning, cytology-based screening programme in which women are invited for a Pap smear every 5 years from age 30 to 60 years.[8]

It is claimed that in future, HPV DNA testing to replace cytology as the primary screening test.[9]However, results from randomized controlled trials show that HPV testing at baseline lead to a lower detection rate of cervical lesions at the next screening round than cytology-based screening.[9]

In reference to above literature research, our study demonstrated the need to incorporate colposcopy and Pap smear in the screening program for early detection and final diagnosis of cervical cancer in Pakistan. Although Pap smears are considered the standard of care for cervical cancer screening in countries with adequate resources, the use of Pap smears alone in our country over the past several decades has

19

failed to lower cervical cancer rates.[3]

In our study, colposcopy and colposcopy directed cervical biopsy proved an effective screening tool, when combined with Pap smear. In our hospital, approximately 3000 Papanicolaou smears are done every year, and incidence of positive smears is approximately 5.7% per 1,000 women, which are comparable to that in other studies. The colposcopy of positive cases is routinely done.

In our study we focused on all women presenting with postcoital bleeding as the primary complaint. The available NICE guidelines state that women with postcoital bleeding should have full pelvic examination, including speculum examination, by the primary health care professional and those patients who have clinical features suspicious of cervical cancer should be referred urgently.[10] A cervical smear test is not required before referral, and a previous negative smear result is not a reason to delay referral.[11] Similarly, the National Health Service cervical screening programme of UK recommends that women presenting with symptoms of cervical cancer such as postcoital bleeding (particularly in women over 40 years) should be referred for gynecological examination and onward referral for colposcopy if cancer is suspected.[12] In our study we recruited ladies only with positive Pap smear. In our study women presenting with postcoital bleeding as the primary complaint showed 8 % prevalence of CIN. Most of these cases had 2.2%CIN3(high grade leisions) which is in contrast to study by R A Saidi where prevalence of invasive cancer was zero.[13] The majority of the women in that study were with a normal-appearing cervix and a prior negative smear test, so showed no underlying significant cervical pathology.

It is clear from the literature that there is variation in the reported prevalence of underlying CIN and cervical cancer in women presenting with postcoital bleeding, with or without normal smears. This could be partially attributed to different populations being studied where risk factors for CIN or cervical cancer vary. In a study for the evaluation of the women who presented with postcoital bleeding by cytology and colposcopy, the sensitivity of colposcopy reported to be 79% by Afsaneh Tehranian.[14]

In our study, the accuracy of the colposcopic directed biopsies is 90.97%, which is comparable to a study by Sukhpreet L Singh i.e., 91%.[15] The sensitivity of this test was 75%, which was comparable to above mentioned.I'They found the positive predictive value of colposcopy to be 36 %, the false positive rate to be 63.64% and the false negative rate to be 42%, which were comparable to those of the present study i.e. 40%, 57.5% and 20% respectively.

In a study by Papa Dasari, with Colposcopically directed biopsies, the incidence of CIN 1 was 13% and that of CIN 2/3 was 11%, which were although more but still comparable to those in the present study i.e. 5.43% and 7.60% respectively.[16]

In another study in which colposcopy was tested for the detection of CIN found the test range of sensitivity of colposcopy for the detection of histologically confirmed low grade cervical intraepithelial neoplasia grade (CIN 1) or high grade cervical intraepithelial neoplasia grade (CIN 2) was 58.0-74.7% and that of specificity was 57.5-92.9%. The sensitivity and specificity of cytology to detect CIN 2 was 57.4% and 99.4%, respectively.[17]

In our study 98% of women with CIN showed acetowhoite areas, which is comparable to the study conducted by Massad in which 93% of women with CIN2+ had at least one acetowhite lesion. Massad in his study concludes that finding acetowhite lesions identifies women with CIN2+, but using subtler colposcopic characteristics to grade lesions is insensitive. Therefore all acetowhite lesions should be assessed with biopsy to maximize sensitivity of colposcopic diagnosis with good specificity.[18]

During colposcopy, the VIA screening was also found more cost-effective than Pap smear screening by an order of magnitude.[19] Population-wide screening with VIA was more costly than screening with Pap smears because more women received treatment. However, the cost per cancer case avoided was far lower because VIA was much more successful at detecting pre-cancerous lesions.[20]

Cytology remains a standardized method for screening for cervical neoplasia but the value of colposcopy is vital in the evaluation of patients with abnormal cervical smears, the false negative cytology results and the poor compliance for follow up. During study it has been felt that apart from cervical smear evaluation, colposcopy should be offered as a diagnostic method in all the patients with unhealthy cervix.

Conclusions

A detailed colposcopic evaluation of the abnormal cervix with a guided biopsy is not only an important diagnostic method for the detection of abnormal or precancerous cells but remains a valuable intervention in planning management and understanding the morphology of the cervical lesions, both the neoplastic and the non-neoplastic. To conclude regular screening of women should be done with Pap smear followed by colposcopy and cervical biopsies of suspicious sites.

Recommendations

Our results are comparable to major published studies. Universal screening is the need of the hour. Improvement in infrastructure, trained personnel, supplies and equipment to enable accurate, reliable and timely testing and reporting of results for one screening visit is required. Many Social factors which influence the outcome in our setting are Illiteracy, lack of awareness, poverty and resorting to alternate medicine which need to be addressed

References

1. Ferlay J, Pisani P. Cancer Incidence Mortality and Prevalence Worldwide, Version 1.0. Lyon: IARC Press; 2007. Review 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests.
2. Wright TC, Massad LS, Dunton CJ, Spitzer M, Wilkinson EJ, Solomon D. 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. Am J Obstet Gynecol 2007; 197:346-55.
3. Bhurgri Y.Karachi Cancer Registry Data--implications for the National Cancer Control Program of Pakistan. Asian Pac J Cancer 2004; 5: 77-82.
4. Wright TC. Cervical Cancer Screening in the 21st Century: Is it Time to Retire the Pap smear? J Clinical Obstetrics & Gynecology 2007 ; 50:313-23
5. Yu CKH. Delayed diagnosis of cervical cancer in young women.J Obstet & Gynecol 2005;4: 367-70.
6. Perkins RB, Langrish M S, Stern J L, Burgess F J, Simon J C. Impact of patient adherence and test performance on the cost effectiveness of cervical cancer screening in developing countries: the case of Honduras.Women;s Health Issue's 2010;20:35-42.
7. Carter R J, Ding Z, and Rose R B. HPV infection and cervical disease: A review. Australian and New Zealand J of Obstet & Gynaecol 2011; 51:

10-38.
8. Rosemelan V J, Kok de Imcm , Ballegooijen V M. Cost-effectiveness of cervical cancer screening: cytology versus human papillomavirus DNA testing. B J Obstet Gynaecol 2012; 119:699-709.
9. Ho CM , Chien YT, Cheng J C, Chang C S, Huang H S. Detection and quantation of human Papilloma virus type 16 , 18 and 52 DNA in peripheral blood of cervical cancer patient. Gynecologiconcology 2005; 99:615-21.
10. Smith R A, Cokkinides V, Brooks D, Saslow D, Brawley O W. Cancer screening in the United States: a review of current American Cancer Society guidelines and issues in cancer screening.Cancer journal for clinicians 2010; 60: 99-119.
11. Kavanagh AM, Santow G, Mitchell H. Consequences of the current patterns of the Pap smear and colposcopy use. J Med Screen 1996; 3:29-34.
12. Arbyn M, Anttila A, Jordan J, Ronco G, Schenck U, Segnan N,Von Karsa L. European guidelines for quality assurance in cervical cancer screening. summary document .Annals of Oncology 2010; 21: 448-58.
13. **Obeidat** R A, Saidi A S**.** Prevalence of High-Grade Cervical Intraepithelial Neoplasia (CIN) and Cervical Cancer in Women with Post-Coital Bleeding (PCB) and Negative Smear: A Retrospective Study Gynecol Obstet 2010; 2:127.
14. Tehranian A, Rezaii N, Mitra M, Eslami B, Arab M, Asgari Z. Evaluation of the women who present with postcoital bleeding by cytology and colposcopy. International Journal of Gynecology and Obstetrics. 2009;105:18-20
15. Singh SL, Dastur NA, Nanavat MS. A comparision of colposcopy and the Papanicolaou smear: sensitivity , specificity and predictive value. Bombay Hospital Journal 2000; 42:3.
16. Dasari P. A grossly abnormal cervix: Evidence for using colposcopy in the absence of a squamous intraepithelial lesion by the conventional Papanicolau's test. Journal of Gynecologic Surgery 2011; 27:1.
17. Pimple SA, Amin G, Goswami S, Shastri SS. Evaluation of colposcopy Vs cytology as secondary test to triage women found positive on visual inspection test. Indian J Cancer 2010;47:308-13
18. Massad LS, Jeronimo J, Katki HA, Schiffman M. The accuracy of colposcopic grading for detection of high grade cervical intraepithelial neoplasia J Low Genit Tract Dis 2009 ; 13:137-44
19. Murillo R, Luna J, Gamboa O, Osorio E, Bonilla J, Cendales R. (2010). Cervical cancer screening with naked-eye visual inspection in Colombia. International Journal of Gynecology & Obstetrics 2010; 109: 230-4.
20. Cagle AJ, Hu SY, Sellors JW, Bao YP, Lim JM, Li SM, et al. Use of an expanded gold standard to estimate the accuracy of colposcopy and visual inspection with acetic acid. Int. J. Cancer 2010; 126:156-61.