Colposcopic Evaluation Of Patients With Abnormal Cervical Cytology And Its Histopathological Corelation – An Original Article

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Citation

Abstract

Diagnosis, management, and follow-up of pre invasive cervical lesions are now a major public health challenge. When a cytologic abnormality is encountered on screening, it has to be confirmed with the help of a conclusive test .Colposcopy and directed biopsy is an accepted management technique for a selected cohort of patients with abnormal cytology. In our study we followed the histopathological outcome of such patients and analyzed the result. MATERIAL & METHODS: Colposcopy and directed biopsy was done. Histological prediction of colposcopic findings done according to the Reid's modified colposcopic index. Colposcopic guided biopsy taken from the most suspicious areas. The result of the biopsy correlated with the predicted diagnosis of Pap smear. The result of the biopsy correlated with the predicted histology of the Reid's modified colposcopic index. RESULTS: Total of 2306 pap smear were taken. Out of these 220 patients had abnormal pap smear (LSIL / HSIL/ASCUS). Colposcopy and directed biopsy was done in 60 patients and histopathology report was collected. The results were analysed statistically. CONCLUSION: Correlation between cytology and HPE was poor as far as mild dysplasias were concerned. But the correlation was good for severe dysplastic lesions. Abnormal Pap smear should be further evaluated in order to get a correct histological diagnosis. Correlation between colposcopic findings and biopsy showed a good correlation for higher grade lesions (CIN III).

INTRODUCTION

Ever since cervical cancer screening with the Papanicolaou smear has become widespread, the incidence of invasive cervical cancer has dramatically decreased. At the same time, the detection of cervical dysplasia has significantly increased (1). Diagnosis, management, and follow-up of pre invasive cervical lesions are now a major public health challenge. For such patients the benefits of detecting and eradicating cervical dysplasia must be balanced against the long-term complications of treatment. The use of the term "pre-cancer" for the low-grade lesions is problematic. Some of the epithelial changes which include the morphological features of neoplasia may, in fact, be acute human papilloma virus (HPV) infections of the epithelium; majority of such lesions will not progress to high-grade intraepithelial neoplasia or to invasive cancer (2).

In the low-grade lesions it is difficult to predict the biological behavior of the epithelial change, but the term "pre-cancer" is still used because of the potential for such lesions to progress to high-grade intraepithelial disease and, subsequently, to invasive cancer.

The optimal screening strategy should identify those cervical cancer precursors which are likely to progress to invasive disease. Also it should avoid detecting transient HPV infection and its associated benign lesions that are not destined to become cancerous. Cytology screening has been very successful in lowering cancer incidence and mortality in countries where good quality screening is available, yet false-positive results are common, since most abnormal cytology is not associated with concurrent CIN3 or cancer (3).

The 2001 Bethesda System terminology is used for cytological classification (4). This terminology utilizes the terms low grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesion (HSIL) to refer to low grade lesions and high-grade cervical cancer precursors, respectively. The histologic classification applies the terms CIN 1 to low-grade lesions and CIN 2, 3 to high grade

precursors. It is important to note that cytological LSIL is not equivalent to histologic CIN 1 and cytological HSIL is not equivalent to histologic CIN 2, 3.

When a cytologic abnormality is encountered on screening, it has to be confirmed with the help of a conclusive test .Colposcopy and directed biopsy is an accepted management technique for a selected cohort of patients with abnormal cytology (5).

In our study we followed the histopathological outcome of such patients and analyzed the result.

MATERIALS AND METHODS

Study population: All women who met the inclusion criterion and gave consent for colposcopy and directed biopsy.

Duration of study: One year from 1st July 2011 to 30th June 2012

Inclusion criteria:

1. Women who have been sexually active
2. 20-60 years of age
3. Women who come as positive for intraepithelial lesions LSIL, HSIL, ASC-US,ASC-H on routine Pap smear.

Exclusion criteria:

1. Women >60 years or < 20 years
2. Women with visibly inflamed or infected cervix.
3. Women with frank cancer.
4. Pregnant women.
5. Post total hysterectomy Patients.

Method

1. Patients meeting the study criterion and who gave consent were recruited.
2. Colposcopy and directed biopsy was done.
3. Histological prediction of colposcopic findings done according to the Ried's modified colposcopic index.
4. Colposcopic guided biopsy taken from the most suspicious areas.
5. The result of the biopsy correlated with the predicted diagnosis of Pap smear.
6. The result of the biopsy correlated with the predicted histology of the Reid's modified colposcopic index.

Colposcopy technique

Method

After introduction of a bivalve speculum, the colposcope was brought into position and focused on the cervix. If there was excess mucus present, it can was removed with a swab dipped in saline. The cervix was then carefully examined prior to application of acetic acid. In some cases, atypical vessels can only be seen before application of acetic acid because of the dense white color that develops after acetic acid is applied.

After thorough inspection, 3% to 5% acetic acid was applied to the cervix with a swab. It takes 30 to 60 seconds for acetowhite changes to occur. Repeated application of acetic acid during the course of the examination is necessary as the acetowhite changes fade within 1 to 2 minutes after application.

Lugol Iodine- Glycogenated cells take iodine, so that they have uniform dark mahogany brown color when stained with Lugol's iodine solution. The normal vaginal and cervical squamous (both native and mature metaplastic) epithelium in women in reproductive age group will take up stain and become brown or black. This is helpful in distinguishing normal from abnormal areas in the transformation zone that have shown faint acetowhitening. Columnar epithelium does not stain with iodine. Immature squamous metaplastic epithelium usually does not stain; sometimes partially stain if it is partially glycogenated. The vascular patterns are difficult to appreciate after application of Lugol's iodine solution. Cervical polyps do not stain with iodine, as they are usually covered with columnar or immature metaplastic epithelium. In postmenopausal women, the ectocervix may not stain fully with iodine due to atrophy of the epithelium.

Satisfactory colposcopy

First, the entire TZ must be seen. This means that 360 degrees of columnar epithelium and 360 degrees of normal squamous epithelium must be seen, as well as all of the area between them. Second, if a lesion is present, it must be seen in its entirety. Lesions that extend up the canal out of sight have not been seen completely. Third, evaluation of the endocervix must be negative. This evaluation includes both visualizing normal columnar epithelium throughout the visible canal, and having a negative sample from the canal.

Biopsy

Biopsy of cervical lesions follows colposcopic evaluation. In

general, the most abnormal lesion was sampled. Depending on the extent of the lesion, one to six biopsies were taken.

Statistical analysis

For statistical analysis data was compiled in Graphpad Prism software and Pearson correlation calculations were done to find out the correlation coefficients using all 3 data sets (Pap smear, colposcopy and histopathological outcome.)

Data table was made by using value given to matched observation.

1 way ANOVA of data table was done using Kruskal-Wallis test and p value obtained.

RESULTS

In this prospective study, eligible women who had abnormal Pap smears were subjected to colposcopy and directed biopsy. The result of histology obtained was analyzed.

Total of 2306 pap smear were taken from 1st July to 30th June which is the time period of our study . Out of these 220 patients had abnormal pap smear (LSIL / HSIL/ASCUS). Colposcopy and directed biopsy was done in 60 patients and histopathology report was collected.

Table 1

The age of the patients

Age in years	ASCUS	LSIL	HSIL
21-30		5	1
31 – 40		15	3
41 – 50		29	1
51 – 60	1	5	0
Total	1	54	5

Majority of patients with high grade lesions were in the 31-40 years age group.

Table 2

Parity of the patients

Parity	ASCUS	LSIL	HSIL
Para 1		10	
Para 2	1	17	4
Para 3		18	1
Para 4		5	
> Para 5		4	
Total	1	54	5

Table 2 shows the parity index of the women included in this study. Women with parity index 2and 3 were 41 (68.33%),

and more than five parity index were 4 (6.66%).

Table 3

Pap smear report (TBS) (4)

Pap smear	RCI (0-2)	RCI (3-4)	RCI (5-8)
ASCUS	1		
LSIL	45	8	1
HSIL			5
Total	46	8	6

Table 3 shows Pap smear findings. Most of the Pap smears were LSIL (90%). But majority of LSIL came in the RCI (0-2) group on colposcopy.

Table 4

Colposcopic impression(RCI)	ASCUS	LSIL	HSIL
0-2	1	45	
3-4		8	
5-8		1	5
Total	1	54	5

100% of high grade lesions corresponded to high grade suspicion on colposcopy. The Low grade lesions mostly turned out to be in the region of 0-2 in the RCI.

After colposcopic assessment, biopsy was taken and sent for histopathological examination.

The biopsies were done in 60 women and the histopathology reports are shown in Table 5.

Table 5

Histopathology report	ASCUS	LSIL	HSIL
Cervicitis/koilocytic atypia	1	52	
CIN I		2	
CIN III			5
Total	1	54	5

Table 6

Correlation between Pap smear and colposcopy

Colposcopy (RCI) Pap smear	0-2	3-4	5-8	Total
ASCUS	1			1
LSIL	45	8	1	54
HSIL			5	5
Total	46	8	6	60

Table 7

Correlation between colposcopy and histology

Colposcopy Histology	0-2	3-4	5-8	Total
Koilocytic Changes/Cervicitis	46	7		53
CIN I		1	1	2
CIN II,III			5	4
Total				60

Table 8

Correlation between pap smear and histology

Pap smear Histology	ASCUS	LSIL	HSIL	Total
Koilocytic Changes	1	52	0	53
CIN I		2		2
CIN II,III			5	5
Total				60

Table 9

Correlation between colposcopy, cytology and histology.

	Colposcopy			Cytology		
	0-2	3-4	5-8	ASCUS	LSIL	HSIL
No CIN	46	7		1	52	
Low grade lesion		1	1		2	
High grade lesion			5			5
Total	46	8	6	1	54	5

Table 10

Correlation and p values

Correlation	Correlation coefficient	P value = < 0.005
Colposcopy versus Cytology	0.553	Yes
Colposcopy versus Histology	0.672	Yes
Cytology versus Histology	0.868	Yes

Correlation coefficient
The correlation coefficient, r, ranges from -1 to +1.

Value of r	Interpretation
1.0	Perfect correlation
0 to 1	The two variables tend to increase or decrease together.
0.0	The two variables do not vary together at all.
0 to -1	One variable increases as the other decreases.
-1.0	Perfect negative or inverse correlation.

Concordance
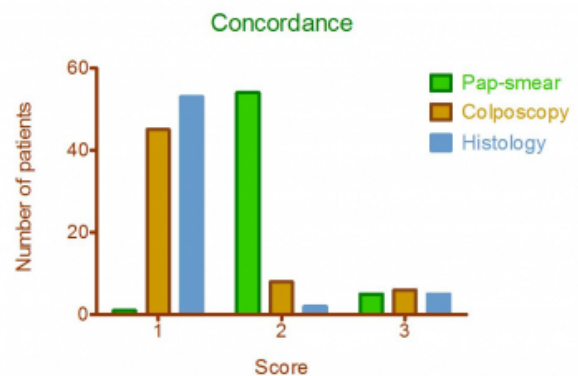
DISCUSSION

The present study was done to correlate the histopathological outcome in case of patients with abnormal cervical cytology tests. This study was done on 60 women who came to Gynae OPD.

Demographic characters:

Age:

In the present study, the maximum number of patients was in the age group of 41-50 years (50%). The predilection for this group for the squamous intraepithelial lesions has been postulated by Rawson et al 1957 (6).

Sedlis et al (1979), stated that the highest rate of dysplasia is found in 20-29 years age group (7).

The mean age of finding squamous intraepithelial lesion is higher in our study than the mean age in other studies. This may be because the patients in our study usually came for other gynaecological problems at a later age and not specifically for screening.

Parity:

68.3% of women in our study were para two or three. All patients of severe dysplasia were multiparous. These are similar to the findings of other authors Christopherson and Parker 1960 (8).

Maliphant (1949), stressed the increasing risk of malignancy with each pregnancy. He found that the risk of malignancy in married women with children was twice as compared to the married women without children and it was ten times more when unmarried women were taken into consideration. (9).

Purandare et al (1977) in their study found a stepwise chronological progression in severity of epithelial abnormalities increasing with abnormal smear in the years of married life. The number of epithelial abnormalities increased with parity (10).

Juneja et al in 1993, did a study concluding that the rate of malignancy was higher in women above 40 years and those with 2 children or more (11).

Sujathan et al concluded that those subjects with a parity of more than 3 and a married life of more than 20 years had a significantly higher number of cytological abnormalities (12).

Epithelial abnormalities:

In the present study, epithelial abnormalities were found in 220/2306 (9.54%) women who had undergone Pap smear

screening.

-- ASCUS was reported 1 case (0.043%
-- LSIL was reported in 214 cases (9.28%)
-- HSIL was reported in 5 cases (0.21%)

5 cases were diagnosed to have HSIL for which cervical biopsy was done. Cervical biopsy revealed CIN3. Cone biopsy was subsequently done in 4 cases and final result also stayed CIN 3. One patient was lost to follow up after doing colposcopic guided biopsy.

One patient had a clinical suspicion of cervical cancer. For her cervical biopsy was taken from OPD itself and which came as squamous cell cancer.

The incidence of dysplasia as reported by ICMR are 15 per 1000 cases screened by cytology and incidence of severe dysplasia detected cytologically is 4-5 per 1000 cases.

In 2003 the median rate of LSIL reported from the College of American Pathology survey was 2.6%. (13).

The rate of LSIL detected in our study is higher as it also included all cases of koilocytosis (according to TBS).

Colposcopic Evaluation

In the present study out of 60 patients, high grade abnormalities (RCI 5-8) were seen in 6 patients (10%) while 8 patients had RCI 3-4(13.3%). The patients with normal colposcopy were 46 (76.6%).

The presence of abnormal colposcopic findings was highest, 100% in cases of HSIL as compared to 16.6% in the LSIL group. The colposcopic findings and cytological findings for high grade lesions were well correlated. But out of all cases of LSIL on cytology only 16.6% showed abnormal colopscopic findings. Therefore false positive rate in low grade lesions on cytology is very high and need further investigation by colposcopic examination.

Stafl and Mattingly examined patients with abnormal Pap smear and found that 46.8% patients had abnormal colposcopy consisting of atypical transformation zone and colposcopy was negative in 40.4% patients (14).

Telebian et al concluded that in case of satisfactory colposcopy the final histological specimen revealed a very high correlation with colposcopy. Where colposcopy was not satisfactory and a diagnostic cone knife biopsy was done, the final diagnosis disclosed a more advanced lesion in 56% of

cases (15).

Selim et al did colposcopic evaluation of abnormal pap smears and found that 59.6% had abnormal colposcopic findings while 32.8% had negative colposcopy findings (16).

Correlation between cytology and histology.

In the present study, out of 60 women 54 had LSIL, 5 patients had HSIL and 1 patient had ASCUS. Out of the LSIL group 52 patients finally had koilocytosis alone while 2 patients had koilocytosis with CIN 1. Above observation shows that the false positive rate for mild dysplasia on cytology is very high and needs further investigation.

Out of the 5 cases of HSIL on cytology all 5 had CIN 3 on histology.

The above reports show that the concordance rate of cytology and histology increases as the grade of diagnosed lesion increases.

Talebian and Shayan showed 100% correlation between cytology and biopsy for high grade lesions (15).

Benedet et al calculated that cytologic-histologic correlation within 1 degree occurred in 82% cases. Cytology underestimated the result of biopsy in 2.3% and overestimated the disease in 16.1% (17).

Creatsas et al found out that 14.3% patients of class 1 Pap smear proved to be dysplasia on biopsy. Dysplasia was found in 41.2% patients of class II Pap smear and 66.7 % of class III Pap smear. 83.3% of class IV smears shows moderate to severe dysplasia on colposcopic guided biopsies (18).

Bolger et al at Watford General Hospital, Hertz performed a prospective study of colposcopy in women with mild dyskaryosis of koilocytosis. The final histological result was CIN III in 22% cases CIN II in 18% cases CIN I in 31% cases and koilocytosis alone in 14% cases and no abnormality in 15%. (19).

Correlation between cytology and HPE was poor as far as mild dysplasias were concerned. But the correlation was good for severe dysplastic lesions.

These studies and the present study clearly shows that abnormal Pap smear has to be further evaluated in order to get a correct histological diagnosis.

Correlation of colposcopy and histology

60 patients with epithelial abnormalities on Pap smear underwent colposcopy and directed biopsy. Biopsy was taken from the most abnormal area.

Colposcopy result was classified according to the modified Reid Colposcopic Index.

Out of the 6 cases that came in the high grade category (RCI 5-8), Histopathology was CIN 3 in 5 cases and CIN 1 in 1 case. 8 cases came in the overlap zone of RCI. Out of these 8 cases 7 were negative for dysplasia while 1 had CIN 1. Colposcopy correctly predicted no lesion in 46 cases which subsequently were found to be negative for dysplasia (CIN) in biopsy. Therefore the correct histological prediction happened in 52 cases out of 60 giving an agreement of 86.6%. 8(13.3%) cases were over reported i.e. histology was less advanced than expected. No case was under reported.

Massad et al in 2002, performed colposcopies on 2825 women. Exact agreement was on 893 women (37%) but results agreed within 1 grade in 75% cases (20).

Boonlikit in 2006, analyzed the correlation and accuracy between RCI and histology result, to differentiate HSIL and LSIL. Overall accuracy was 89% (21).

Stafl and Mattingly found correlation between colposcopy and histology to be 85%. Histology was less advanced than expected in 11.7% cases and more advanced than expected in 3.3% cases (22).

Javaheri et al did colposcopy and directed biopsy on patients with abnormal Pap smears. They achieved a histological correlation of 85.9% in high grade lesions and a correlation of 95.9% in low grade lesions. 12.2% patients had less advanced histological diagnosis in the high grade lesion group (23).

Correlation between colposcopic findings and biopsy showed a good correlation for higher grade lesions (CIN III). Pap smear correctly identified all the 5 high grade lesion while colposcopy shortlisted 6 lesions and out of which there were 5 true positive for high grade lesions.

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