

Cytopathology of Cervix with particular reference to Sexually Transmitted Diseases

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Abstract: With the increased incidence of STDs and cervical cancer, lifetime screening for every women between the age group of 21 – 40 years appears to be the best approach at this moment. Screening of high – risk cases like HIV and other STDs is a must.

In the present study non – viral STDs constituted 80% mixed infection 14% and viral STDs 6% which were detected on cervical cytology only. Associated squamous intraepithelial lesions constituted about 30% with nil incidence of invasive carcinomas, establishing the fact that it takes over a decade for invasive carcinoma to develop. In this study, 71 cases were HIV seropositive, with two cases (2.8%) showing invasive carcinoma in asymptomatic women and 11.2% with squamous intraepithelial lesion. Hence HIV is a likely risk factor in the etiopathogenesis of cervical cancer if the patient survives longer.

Keywords: STD, Bethesda system, Squamous intraepithelial lesion.

I. Introduction

Cervical cancer is one of the most common neoplastic diseases affecting women, with a combined worldwide incidence exceeded only by breast cancer and colorectal cancer. It comprises about 9.8% of all cancers worldwide, accounting for about 80% of all genital tract cancers in India.

According to available WHO data, there are 10 million new cases, 6 million deaths and 22 million people living with cervical carcinoma globally. In India 1, 25, 952 new cases are being added per year.

In many areas where the cancer cervix is already high, large number of women are now infected with HIV, raising the possibility that incidence of cancer cervix may further increase. Cancer cervix is regarded as one of the case defining conditions of AIDS, according to 1993 revised terminology for AIDS.

There is significant relationship of STDs with development of cervical cancer especially in the pre-invasive phase. Hence cytological detection of STDs should be mandatory in a cytological surveillance programme to check the onset and progress of the disease.

The present study was undertaken to know the efficacy of cervical cytology in the detection of STDs either by the identification of the organisms or by their characteristic cytological cellular changes and to establish the early diagnosis of cervical cancer. "The Bethesda System, 2001" was used for cervical cytological reporting.

Aim of the study is to detect association between sexually transmitted diseases and cytopathological changes in cervical epithelium and to detect cancer cervix at an early stage.

II. Material And Methods

A total number of 200 women attending the out patient department of STD were taken up for the study. Some of the patients were asymptomatic while others were referred from other O.P and peripheral Hospitals with vaginal discharge, cervical erosion, post-coital bleeding ,intermenstrual bleeding and pain abdomen.

A complete case history of the patients was taken with reference to her marital status, socioeconomic status, previous H/O exposure to STDs, male partner having STD, pregnancy, usage of any contraceptives and menstrual history with LMP.

General examination for evidence of cachexia, lymphadenopathy and organomegaly was done. Serological tests for HIV and VDRL were done in all cases examined. Taking universal precautions, speculum examination with Sim's speculum done and vaginal discharge was collected for wet mount and gram stain. Immediately, their results were noted down.

After wet mount, Cervical scrape smear from SCJ was obtained with Ayre's spatula ,stained according to Papanicolau's technique and H&E.

Biopsy was taken in cases of chronic infections, dysplasia and frank cancer. Punch biopsy was taken from suspected areas of cervix, fixed in 10% formalin. Paraffin embedded sections were stained with H & E stain, PAS & Reticulin stain. PAS Stain was used to differentiate adenosquamous pattern from squamous pattern. Reticulin and PAS stains were used to know the invasion of basement membrane.

The results of cytology and biopsy were analysed according to the Bethesda system 2001, independently and the results were correlated. Bethesda report format/table

Results

Total number of women screened : 200
 Total number of adequate Pap smears obtained : 196 (98%)
 Total number of cases available for correlation with HPE : 128
 Number of STDs diagnosed on cervical cytology : 50 (25%)
 Number of cases available for correlation with HPE in STDs : 33
 Number of HIV seropositive cases : 71 (35.5%)
 Number of cases available for correlation with HPE in HIV : 21 (10)

III. Figures and Tables

Tab.1 Risk Factors Associated With Cervical Lesions

S.No.	Risk Factor	No. Of Cases (N-200)	%
1	Low Socio Economic Status	196	98
2	Early Age At Marriage	182	91
3	Multi Para	101	50.5
4	H/O Std	71	35.5
	• Hiv	32	16
	• Other Stds		
5	Male Factor	52	26
	• Male Std	2	1
	• Circumcision Done		
6	Pregnancy	1	0.5
7	Smoking	Nil	Nil

Most of the cases had multiple risk factors which were interrelated.

Table . 2. STDs Diagnosed On Cervical Smears

Type Of Stds	No. OF Cases (N-50)	%
Trichomonas Vaginalis	31	62
Candida Albicans	9	18
Mixed (TV & CA)	7	14
Herpes Simplex Virus	1	2
Human Papilloma Virus	2	4
TOTAL	50	100

Table. 3. Relation of STDs with Age

S.No.	AGE GROUP (Years)	No.OF CASES (N-50)	TYPE OF Stds				
			HSV (N=1)	HPV (N=2)	TV (N=31)	CA (N=9)	MIXED TV & CA (N=7)
1	< 20	9 (18%)	-	-	6	1	2
2	21-30	26 (52%)	1	1	12	8	4
3	31-40	13(26%)	-	1	11	-	1
4	41-50	2(4%)	-	-	2	-	-

Table. 4. Relation of STDs with gynaecological symptoms

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S.No.	COMPLAINT	No. OF CASES (50)	HSV (n=1)	HPV (n=2)	TV (n=31)	CA (n=9)	MIXED TV & CA (n=7)
1	White Discharge	43 (86%)	1	2	25	8	7
2	Irregular periods	1 (2%)	-	-	1	-	-
3	Asymptomatic	4 (8%)	-	-	4	-	-
4	Pain abdomen	1 (2%)	-	-	-	1	-
5	Post coital bleeding	1 (2%)	-	-	1	-	-

Table. 5. Association Of STDs With Clinical Lesions Of Cervix

S.No.	Complaint	No. OF CASES(50)	TYPE OF Stds				
			HSV (N=1)	HPV (N=2)	TV (N=31)	CA (N=9)	MIXED TV & CA (N=7)
1	Erosion	40 (80%)	1	-	25	7	7
2	Hypertrophy	1 (2%)	-	-	-	1	-
3	Bleeding On Touch	2 (4%)	-	-	1	1	-
4	Healthy Cervix	6 (12%)	-	1	5	-	-
5	Warts	1 (2%)	-	1	-	-	-

Table.6. Analysis Of Cervical Lesions On Cytology In STDs

S.No	TYPE OF STD	No. OF CASES(50)	CERVICAL LESION			
			Neg. For IEL	LSIL	HSIL	Carcinoma
1	TV	31	24 (77.4%)	6 (19.4%)	1 (3.2%)	-
2	CA	9	5 (55.6%)	4 (44.4%)	-	-
3	Mixed TV&CA	7	6 (85.7%)	1 (14.3%)	-	-
4	HSV	1	-	1 (100%)	-	-
5	HPV	2	-	1	1	-

			(50%)	(50%)	
TOTAL	50	35	13	2	Nil

Table.7. Correlation Of Cervical Lesions In STDs

Cervical lesion on cytology	No. of cases(33)	No. of cases correlated with HPE	%	No. of cases not correlated with HPE	%
Neg.for IEL	21	20	95.2	1	4.8
Epithelial Abnormality					
LSIL	11	6	54.5	5	45.5
HSIL	1	1	100	-	-
TOTAL	33	27	81.8	6	18.2

Table.8 Cervical Lesions Seen On Cytology In Hiv Positivecases – 71.

S.No.	Type Of Lesion	No. Of Cases	%
1	With In Normal Limits	13	18.3
2	Negative For Intraepithelial Lesion	48	67.6
	➤ Non Specific Infection	28	39.4
	14		
	3		
	➤ Specific Infection	2	
	1		19.7
	• Trichomonas Vaginalis		4.2
	• Candida Albicans		2.8
	• Mixed Tv And Ca		1.4
	• Tuberculosis		
3	Epithelial Abnormality	3	4.2
	• Low Grade Squamous Intra Epithelial Lesion	5	7.0
	• High Grade Squamous Intra Epithelial Lesion	2	2.8
	Carcinoma		
	Total	71	100%

Table.9 Cervical Lesions On Cytology In Non -Hiv Cases

S.No	Type Of Lesion	No. Of Cases(125)	%
1	With In Normal Limits	5	4
2	Negative For Intraepithelial Lesion	61	48.8
	➤ Nonspecific Infection	45	36
	➤ Specific Infection		
	• Trichomonas Vaginalis	10	8
	• Candida Albicans	2	1.6
	• Mixed Tv And Ca	4	3.2

3	Epithelial Abnormality	59	47.2
	➤ Squamous Cell:		
	• Ascus	2	1.6
	• Lowgrade Squamous Intra Epithelial Lesion	16	12.8
	• Highgrade Squamous Intra Epithelial Lesion	14	11.2
	• Carcinoma	23	18.4
	➤ Glandular Cell	1	0.8
	• Agc	1	0.8
	• Ais	2	1.6
	• Carcinoma		
Total		125	100

Table.10 Correlation Of Cervical Lesions On Cytology With HPE In HIV & Non - HIV Cases

Cases	Total no. of cases	No. of cases correlated with HPE	%	No. of cases not correlated with HPE	%
HIV	21	19/21	90.5	2/21	9.5
Non-HIV	107	81/107	75.7	26/107	24.3
TOTAL	128	100/128	78.1	28/128	21.9

Table.11 Correlation Of Cervical Lesions On Cytology With HPE in HIV Cases

Cervical lesion on cytology	No. of cases	No. of cases correlated with HPE	%	No. of cases not correlated with HPE	%
Neg.for IEL	15	14	93.3	1	6.7
Epithelial abnormality					
LSIL	2	1	50	1	50
HSIL	2	2	100	-	-
Carcinoma	2	2	100	-	-
TOTAL	21	19	90.5	2	9.5

Table.12. Correlation of cervical lesions on cytology with HPE in non - HIV cases 107cases

Cervical lesion on cytology	No. of cases	No. of cases correlated with HPE	%	No. of cases not correlated with HPE	%
Neg.for IEL	49	47	95.9	2	4.1
Epithelial abnormality					100
ASCUS	2	-	-	2	68.5
LSIL	16	5	31.2	11	69.2
HSIL	13	4	30.8	9	-
Carcinoma	25	25	100	-	100
AGC	1	-	-	1	100
AIS	1	-	-	1	
Total	107	81	75.7	26	24.3

Figure: 1



Figure: 2



Figure: 3

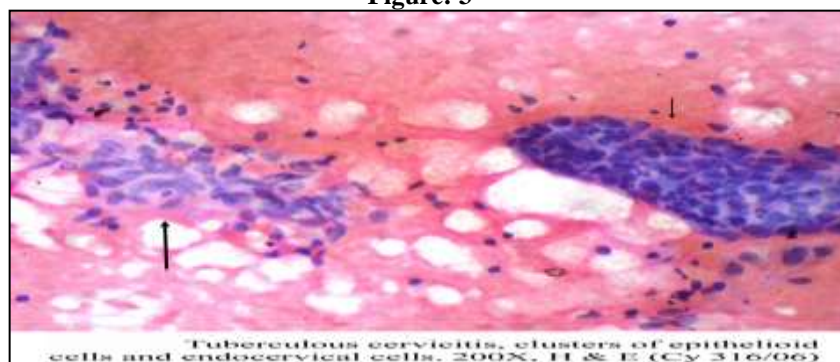


Figure:4

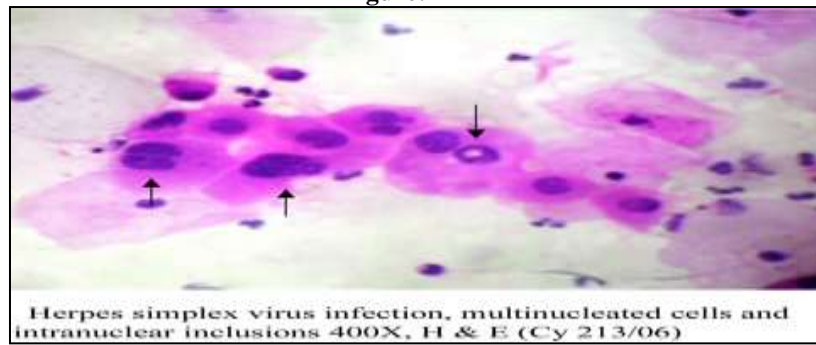


Figure:5

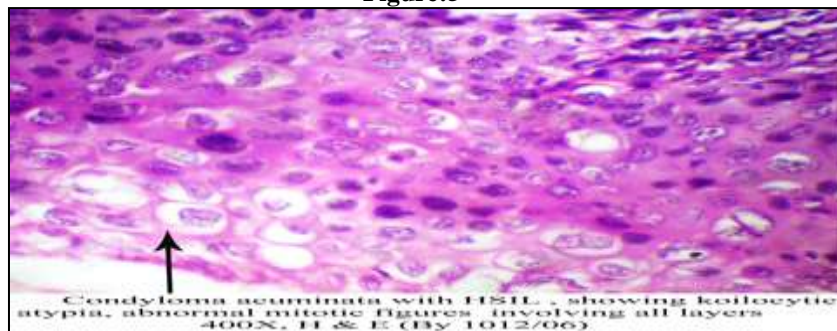


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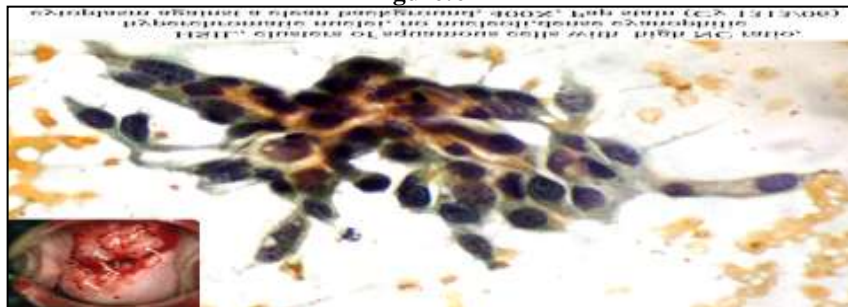
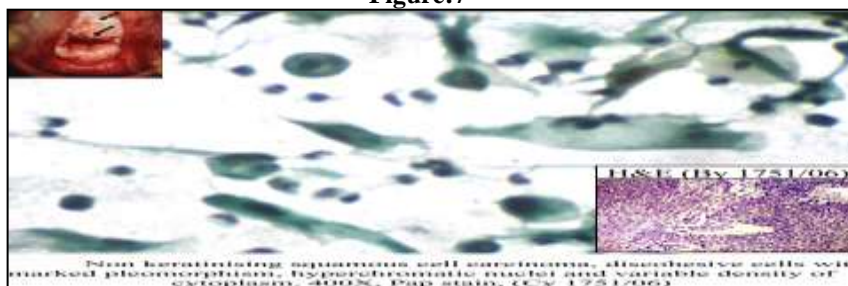


Figure:7



IV. Discussion

Cervical screening using Papanicolaou test is an effective, low cost screening test for the detection of STD agents, precancerous and cancerous lesions of the cervix. As there is significant relationship of STDs with development of cervical cancer especially in the pre-invasive phase, cervical cancer is considered as an STD (K.K. Holmes, Richard M Briggs).Cancer Cervix is associated with sexual activity and was noted by Rigoni – Stern in 1842. Prevalence studies indicate that precursor lesions of cancer cervix occur approximately 5 times more frequently among women attending STD clinics than those attending Family Planning clinics.

In the present work an attempt was made to know the efficacy of cervical cytology in diagnosing STDs by either identification of the organisms or of their characteristic cytological cellular changes in 200 women attending STD clinic. Several risk factors involved in etiopathogenesis of cervical neoplasia were analysed .

Most of the cases had multiple risk factors, which were interrelated. The commonest being low socio economic status 98%, early age of marriage less than 20 yrs 91%, multi-parity (more than 4 children) 50%, HIV seropositive 35.5% cases and 16% associated with other STDs. LN Biswas, B. Manna et al confirmed the association of early age at first coitus and cervical cancer in women. Reid et al (1978) observed that males of low socio economic strata have high protamine content in their sperm, which was responsible for cervical neoplasia. Abeyewikreme et al stated that women with five or more pregnancies had higher incidence of abnormal smears than normal. In the present study 50 STDs diagnosed on cervical smears were analysed and compared with other studies.

Table: 13 comparison of various stds in the present study with other studies

S. No.	Various Studies	Types Of Stds			
		Tv	Ca	Hsv	Hpv
1.	J.S. Misra Et Al (2004)	55.9 %	27.5 %	6.5 %	10.02 %
2.	Veena Kashyap Et Al (2002)	67.8 %	7.6 %	0.57 %	10.7 %
3.	Present Study (2006)	62 %	18 %	2 %	4 %

Relationship of the four STDs with squamous intraepithelial lesions of cervix and carcinoma cervix was analysed and compared with other studies. The analysis also included, common age at presentation along with clinical symptoms and signs. Of the 5 cases presented with external genital warts, 3 were associated with STDs on cervical cytology.

In the present study commonest age group was 21 – 40 yrs, with 2 cases belonging to the age group between 41 – 50 yrs. It is a common notion that STDs are uncommon in the peri-menopausal and post menopausal age group, but Veena Kashyap et al and Konje JC et al stated that women in the age group of 41 – 50 yrs are relatively sexually active and hence are prone to STDs.

Table: 14. Comparison Of Age Distribution Of STDs With Other Studies

S.No.	Author (Year)	Number Screened	Most Common Age Group Affected (Years)
1.	Misra Et Al (2004)	1477	21 – 40
2.	Abeye Wickreme	350	< 35
3.	Konje Et Al (1989)	322	30
4.	R M Briggs Et Al (1980)	764	23.8
5.	B.A. Kelly Et Al	826	38
6.	Present Study (2006)	200	21 – 40

In the present study majority of cases were non-viral STDs, out of which Trichomonas vaginalis was the commonest. Majority of the STDs presented with white discharge in the present study when compared to that of Misra et al study, which were mainly asymptomatic. The reason could be due to illiteracy and lack of awareness of the screening programmes, hence attending the clinic only when they were symptomatic. In the present study the sample size being small the analysis of viral STDs were difficult to compare with other studies.

In the present study of 200 cases screened, 71 were infected with HIV and 129 were uninfected with HIV. Out of the 71 HIV seropositive cases, 48 / 71 (67.6%) were negative for intraepithelial lesion. 10 / 71 (14.1%) showed epithelial abnormality. LSIL was seen in 3 / 71 (4.2 %), HSIL 5 / 71 (7%) and invasive carcinoma in 2 / 71 (2.8%). Out of 129 cases which were negative for HIV, only 125 cases were available for interpretation. 61 / 125 (48%) were negative for intraepithelial lesion. 59 / 125 (47.2%) showed epithelial abnormality.

LSIL was seen 16 / 125 (12.8%), HSIL 14 / 125 (11.2%) and invasive carcinoma 25 / 125 (20%), 2 cases of ASCUS and 2 cases of Atypical glandular cells.

Table:15.Incidence of SIL and invasive Carcinoma in HIV infected women, comparison with other studies.

S. No.	Various Studies	No. of Case	Epithelial abnormality		
			LSIL	HSIL	Invasive Ca.
1.	Tedd. V. Eller Brock (2000)	HIV + (328)	91%	-	-
		HIV - (325)	75%	-	-
2.	Present Study (2006)	HIV + (71)	4.2%	7%	2.8%
		HIV - (129)	12.8%	11.2%	20%

In the present study it has been observed that HIV is a likely risk factor in causing cervical cancer. But our current inability to demonstrate the increased risk of HIV in causing cancer cervix, could reflect the fact that HIV infected women are dying of other opportunistic diseases before their cervical cancer develops or is detected. (Nancy B. Kiviati). Total number of cases available for correlation of cytological changes with HPE out of 200 cases screened were 128. Correlation was seen in 100/128 (78.1%). In HIV seropositive cases, 19/21 (90.5%) and in non HIV cases 81/107 (75.7%), correlation was seen. In STD cases 27/33 (81.3%) showed correlation, 7/12 (58.3%) cases of STDs with SIL showed correlation.

Table:16. Percentage Correlation Of SIL In STDs in the Present Study with those Of Others

S. No.	Various studies	% correlation of SIL in STDs
1.	Misra et al (2004)	80%
2.	RM Brigg's (1980)	61%
3.	Present study (2006)	100%

Out of 128 cases including both HIV and non-HIV cases, 64 cases showed epithelial abnormality. Out of 64 cases with epithelial abnormality, 39(60.9%) were correlated, 25 / 64 (39.1%) did not show correlation.

The analysis of these 25 deferral cases was as follows :

6 cases of HSIL on cytology proved to be non keratinizing SCC on histopathology. The nuclear features of carcinoma are similar to that of HSIL. The only differentiating feature being presence of tumor diathesis. In some of the invasive carcinomas tumor diathesis is not seen, hence tendency to under diagnose the lesion. 2 cases of LSIL on cytology turned out to be inflammation with repair on HPE. Nuclear enlargement and presence of nucleoli can be alarming, favoring the diagnosis of LSIL and difficult to differentiate from repair. 2 cases of atypical glandular cells favouring neoplasia, were under diagnosed due to lack of tumor diathesis. They were adenocarcinoma on HPE. Invasive endocervical carcinoma can show cytologic features similar to AIS and in some cases the two entities may be difficult, if not impossible, to separate (Atkinson). 2 cases of HSIL were over diagnosed on cytology due to inflammation, but however repeat smear was advised. 2 cases with diagnosis of LSIL on cytology turned out to be carcinoma on HPE, probably due to sampling error.

8 cases of LSIL with associated infection like Trichomonas, candida and mixed infection showed chronic nonspecific cervicitis on HPE. LSIL was over diagnosed on cervical cytology associated with inflammatory changes. However patients were advised for repeat smear after a course of antibiotic therapy but they did not turn up. 1 case Trichomonas infection on cytology was within normal limits on HPE, probably Trichomonas could be a commensal.

V. Conclusion

Cytology is definitely a major screening method for the detection of cervical lesions. Cytology supplemented with HPV-DNA detection test will be more effective in screening programs. Effective screening would lead to early detection and management of cervical cancer.

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