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Role of PAP smear N cervical biopsy in unhealthy cervix

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Abstract

Carcinoma of cervix is the third most common cancer in women worldwide & most common female cancer in many developing countries like India. The present study was done with an objective to correlate the finding in women with unhealthy cervix by cytology and cervical biopsy and to assess the utility of these in detecting the premalignant and malignant lesions of the cervix. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of Pap smear were compared with cervical biopsy which was taken as confirmatory. Majority of patients were from age group of 31- 40 years (41%). The mean age of cervical intraepithelial neoplasia (CIN) and invasive carcinoma are 50.6% and 49.37%. Majority of cases with abnormal cervical lesion were in the multiparous women (parity from 2 to 4) which constituted 88 (73.34%) cases out of 120 cases. The mean parity of neoplastic lesions was around 3.35 and for invasive carcinoma it was around 4.42 in the present study. The incidence of CIN (45%) and invasive carcinoma (77.14%) was found to be higher among the low socio- economic group. CIN and invasive carcinoma was more prevalent among the illiterates, in the study 50% of CIN and 57.15% of invasive carcinoma cases was found among the illiterates. The incidence of CIN was 40% and of invasive carcinoma was 67.18% in women who were married before 20 years of age. Majority of women complained of excessive white discharge per vaginum (68.34%) and among them 13.12% (16/82) of women had CIN. In the present study 94% cases of postmenopausal bleeding were diagnosed to have CIN and invasive carcinoma and 51.54% cases of irregular bleeding were diagnosed to have CIN and invasive carcinoma. The gross appearances of cervix revealed cervical erosion in 38.34% (46/120) of cases, rest of the cases showed growth in 27.5%, congestion in 10%, Hypertrophy with congestion seen in 5.84%, Hypertrophy with erosion was seen in 11.66% and polyp was found in 4.16% of cases. Majority of cases with invasive carcinoma showed growth in the cervix (94.2% cases). In the present study pap test revealed inflammatory smears in 55% of cases, mild dysplasia in 5.84%, moderate dysplasia in 6.66%, severe dysplasia in 5.84% and invasive carcinoma was seen in 22.5% of cases. Sensitivity of pap smear was 86.5% and specificity was 92.18% in the present study. The positive predictive value was 90.7% and the negative predictive value 89.4 %. The accuracy of pap smear was found to be 90%.

Keywords: PAP smear, Cervical intraepithelial neoplasia, Sensitivity, Specificity.

Introduction

Carcinoma of cervix is the third most common cancer in women worldwide & most common female cancer in many developing countries like India.[1] Incidence of preclinical and invasive carcinoma is undeniably high amongst the group of "unhealthy cervix". Incidence of invasive carcinoma is reported to be 29 / 1000 in women with abnormal cervix but only 1.53 per 1000 in those with a healthy cervix.

Incidence of invasive carcinoma shows gradually decreasing trend because of advancement of various methods for early detection. Again early detection in preclinical stage ensures 100% survival rate. The ultimate aim of various modalities of diagnosis is to prevent the development of invasive cervical cancer. Out of various available methods cytology, coloposcopy & histopathology are most commonly used worldwide at present.

Clinical utilization of cytopathology is rapidly expanding and exfoliative cytology in early detection of cervical cancer has become firm established. It gives the first signal to the need further essential diagnostic procedures and then evaluates their accuracy. By its use appropriate treatment is indicated initially and evaluated for efficacy subsequently**.**

Pap smear was first described by Papanicolaou and Traut in 1943. Aside from pre malignant & malignant changes other local conditions can often be recognised by the cytologist.[2] Pap smear is a screening test only. Positive test requires further investigation like coloposcopy, cervical biopsy and fractional curettage. Pap smear can detect 98% of cancer of the cervix and about 70% of endometrial cancer. Reliability of the report depends upon the slide preparation and skill of cytology. Whereas single test yields as much as 10 – 15% false negative reading, it is reduced to only 1% with repeated test.

Diagnosis can only be made for certain by microscopic examination of cervical tissue. Biopsy is essential in every case where signs or symptoms raise the slightest suspicion and it is irrespective of whether cervical smear contain malignant cells. Either punch or wedge or cone biopsy can be taken depending upon lesion and involvement. Keeping the above facts in view, the present study is designed to evaluate the role of pap smear and biopsy in a women presenting with unhealthy cervix.

Material and Methods

This study was conducted in the department of obstetrics and Gynaecology at a tertiary care hospital from October 2010 to September 2012. This was a prospective clinical study conducted in Out Patients Department (OPD) or being admitted to indoor ward. Among them women who fulfilled selection criteria were randomly selected. Written and informed consent were obtained from all the participants after brief explanation of the procedure.

Inclusion criteria

1. Married women
2. Patients with abnormal symptoms like profuse white discharge, post coital bleeding, irregular bleeding or post menopausal bleeding.
3. Patients with clinically unhealthy cervix diagnosed by speculum examination like cervical erosion, congestion, hypertrophy, ectropion, cervical polyp and growth.
4. Patients with pap smears showing dysplasia

Exclusion criteria

1. Unmarried women
2. Patients with bleeding at the time of examination
3. Women who underwent total hysterectomy
4. Pregnant women

After preliminary inspection of the cervix, a Pap smear was taken using Ayre's spatula. The squamo - columnar junction was scraped with the Ayre's spatula by rotating full 360 degree. The scrapings were evenly spread on a glass slide and immediately fixed by dipping in the jar containing equal parts of 95% ethyl alcohol and ether and transported to the cytopathological laboratory. Smears were analyzed by senior pathologist. The Richart's classification was used for describing Pap smear results.

Bimanual examination:

A bimanual examination was done to know position, size of the uterus, feel of cervix and to find if there is any tenderness, induration or mass in the fornices.

Cervical biopsy:

Biopsy was taken from abnormal area, in the form of either a cervical punch or wedge or cone biopsy in operation theatre under anaesthesia. The specimen was sent for histopathological examination in 10% formalin solution. Slides were analyzed by senior consultant pathologist.

Biopsy results were categorized as

1. Cervicitis/ metaplasia
2. CIN-1 (mild dysplasia/ correlating with LSIL)
3. CIN-2/3 (moderate to severe dysplasia/ correlating with HSIL)
4. Squamous cell carcinoma

Results

A total of 120 participants were included in the study. The maximum number of cases i.e. 41 cases (34.2%) were found in 31–40 years age group. There were 36 cases (30%) in age group of 41–50 years. Age distribution of the different cervical neoplasia among the patients, it was seen that the mean age of CIN as a whole is 47.5years, whereas mean age of invasive carcinoma is 49.4 years.

Majority of cases with abnormal cervical lesion were in the multipara group (parity from 2 to 4) which constituted 88 (73.4%) cases out of 120 cases. All cases of neoplastic changes are seen after parity 2 and above. The mean parity of neoplastic lesions was around 3.35. Most of the cases in this study are from lower socio-economic status (63.34%). The richer society contributes 3.33% of cases. In the present study it was shown that CIN and invasive carcinoma were common in low and middle socioeconomic status.

Out of 36 invasive carcinoma cases 28(77.8%) were found in low socio economic class. Among 120 women studied, 29.16% were illiterates, 62.5% had primary/high school education and 8.34% had Higher education. Among the total CIN cases 50% were illiterates, 40% studied up to high school and 10% had their higher education. Among the total invasive cases 58.34% were illiterates. Among 120 women , 70 cases (58.3%) when they were less than 20 years of age, 35 cases (29.2%) at 21 to 25 age group, 10 cases (8.3%) at 26 to 30 age group and 5 cases (4.2%)

at 31 or above group. Among 20 CIN cases 45 % were less than 20 years of age. Among 36 invasive carcinomas, 86.1% cases married at a young age of less than 20 years.

The distribution of cases according to the symptoms is shown in table1.

Table 1: Distribution of cases as per symptoms

Symptoms	No. of cases	Percentage
Whitish discharge	82	68.3%
Irregular bleeding	62	51.7%
Post menopausal bleeding	17	14.2%
Post coital bleeding	10	8.3%
Blood stained discharge	6	5%
Menorrhagia	12	10%
Low backache	17	14.2%
Others	6	5%

Whitish discharge was the main complaint of maximum no of patients with unhealthy cervix and represented 68.3% followed by irregular bleeding (51.7%). Among 120 cases 17 (14.2%) presented with post menopausal bleeding, 10 (8.3%) with post coital bleeding, 12 (10%) menorrhagia and low backache in 17 cases (14.2%).

The gross appearance of cervix is shown in table 2.

Table 2: Gross appearance of cervix

Appearance of cervix	No. of cases	Percentage
Erosion	46	38.3%
Congestion	12	10%
Hypertrophy + erosion	16	13.4%
Hypertrophy+congestion	7	5.8%
Hypertrophy + ectropion	1	0.8%
Mucus Polyp	5	4.2%
Growth	33	27.5%
Total	120	100%

Maximum number of cases showed erosion 51.7% which was followed by growth in 27.5% cases. Hypertrophy with erosion was seen in 13.4% 0f cases, hypertrophy with congestion in 5.84%, congestion in 10% and mucus polyp was seen in 4.16% of cases.

The relation between gross appearance of cervix and cervical neoplasia is shown in table 3.

Table 3: Relation between gross appearance of cervix and cervical neoplasia

Gross Appearance	No. of cases	CIN					Invasive Carcinoma	
		I	II	III	Total	Percentage	Number	Percentage
Erosion	46	2	4	4	10	50%	-	-
Congestion	12	2	1	-	3	15%	-	-
Hypertrophy + erosion	16	-	1	3	4	20%	3	8.33%
Hypertrophy + congestion	7	-	1	2	3	15%	-	-
Hypertrophy + ectropion	1	-	-	-	-	-	-	-
Ulcerative Growth	33	-	-	-	-	-	33	91.67%
Polyp	5	-	-	-	-	-	-	-

Out of 20 CIN cases, 70% showed erosion in the gross appearance of cervix. Out of 35 invasive carcinomas 91.67% of cases showed growth in the cervix.

The pap smear findings are shown in table 4.

Pap smear revealed that 55% had an inflammatory/metaplasia and 22.5% showed invasive carcinoma. Among 27 positive cases for cervical neoplasia, 5.8% had CIN I changes, 9.2% had CIN II changes and 7.5% had CIN III changes.

The histopathological findings are shown in table 5.

Table 4: Pap smear findings

Pap smear	No. of cases	Percentage
Inflammatory / metaplasia	66	55%
CIN I	7	5.8%
CIN II	11	9.2%
CIN III	9	7.5%
Invasive carcinoma	27	22.5%
Total	120	100%

Table 5: Histopathological findings

Histopathology findings	No of cases	Percentage
Normal	6	5%
Cervicitis / metaplasia	53	44.16%
CIN I	4	3.34%
CIN II	7	5.84%
CIN III	9	7.5%
Invasive carcinoma	36	30%
Mucus polyp	5	4.16%
Total	120	100%

All 120 cases were subjected to either punch, wedge or cone cervical biopsy or endometrial curettage. Majority of cases, 44.16% had chronic cervicitis, 4.16% had mucus polyp, 3.34% had mild dysplasia, 5.84% had moderate dysplasia and 7.5% had severe dysplasia. In 30% cases HPE revealed invasive carcinoma.

The cytohistological correlation is shown in table 6.

Table 6: Cytohistological correlation

Pap Smear finding	Biopsy finding			
	Normal/Polyp	Inflammatory	CIN	Invasive Ca.
Inflammatory	11	48	7	-
CIN	-	5	12	10
Invasive Ca.	-	-	1	26

The diagnostic efficacy of Pap smear is shown in table 7.

Table 7: Diagnostic efficacy of Pap smear

Diagnostic Efficacy	Percentage
Sensitivity	86.5 %
Specificity	92.18%
Positive predictive value	90.7 %
Negative predictive value	89.4 %
Accuracy	90%

Pap smear showed sensitivity of 86.4% and specificity 92.18% in detecting cervical neoplasia and malignancy. The overall accuracy was 90%.

Discussion

Invasive cancer of cervix is considered to be a preventable condition as it is associated with a long pre invasive stage (CIN) making it amenable to screening and treatment. The incidence of cervical cancer can be reduced by as much as 80% if the quality, coverage and follow- up of screening methods are of high standard.

Frequently repeated cytology screening programs have led to a large decline in cervical cancer incidence and mortality in developed countries. Cytology based screening programs have achieved very limited success in developing countries like India due to lack of trained personnel, laboratory facilities, equipments, high cost of services and poor follow-up. It has become necessary to find out alternative screening procedure to cytology which has high sensitivity and specificity.[3]

Maximum number of cases of unhealthy cervix were in the age group of 31- 40 years (41%) and the mean age was found to be 44.18 years. It confirms the well established fact that, unhealthy cervix is more common in women of reproductive age group who are sexually active. Sandhya (2009), Ashfan (2010) and Bhojani KR *et al* (2011)[4] showed that majority of cases of unhealthy cervix are in the age group of 31–40 years, which is consistent with the present study.

The mean age distribution for CIN as a whole was 50.6 years and that of invasive carcinoma was found to be 49.4 years in the present study. It has also been observed that there was chronological progression in time from CIN I (mean age 46.5) to CIN II (mean age 47.8 years) and CIN III (mean age 48.2 years) which is in ascending order. Similar progression in time has been observed by Meisels A *et al* (1969).[5] This observation also supports that CIN is a continuous process which begins in its morphologically identifiable stage as CIN I or mild dysplasia and ends in invasive carcinoma.

We have got maximum vulnerability of invasive cervical cancer in age group of 41 to 50 years. In the present study the mean age of invasive cervical cancer was 49.4 years and according to Jemal A *et al* (2002)[6] the mean age was 52.2 years, Bhojani KR et al (2011) [4] it was 60 years and MS Bal *et al* (2012)[7] it was 57 years. The age group and mean age of invasive carcinoma in the present study were found to be lower as compared to other authors.

Majority of cases with abnormal cervical lesion were in the multiparous women (parity from 2 to 4) which constituted 88 (73.4%) cases out of 120 cases. None of the cases of neoplastic lesion was seen in nulliparous or primiparous women. Both Kushtagi P *et al* (2002)[8] and Vaidya *et al* (2003)[9] also showed that the prevalence of CIN was significantly higher in parity of more than 2 and parity more than 4 respectively.

The mean parity of neoplastic lesions was around 3.35 and for invasive carcinoma was around 4.42 in the present study. The study done by Shalini *et al* (1998)[10] showed that the mean parity was 4.2 in patients with invasive cancer, which is consistent with the present study. The correlation of multiparity and cervical neoplasia may be attributed to hormonal and nutritional changes that occur in pregnancy, immuno suppression during pregnancy, and cervical trauma during vaginal delivery (Adadevoh *et al*)[11].

Socio economic status had always been playing an epidemiological role in genesis of dysplasia. In the present study, the incidence of CIN (45%) and invasive carcinoma (77.14%) was found to be higher among the low socio- economic group. Vaidya *et al* (2003)[9] had showed that low socio economic status had a definite role on the development of dyskaryosis. In his study 80% of CIN I and 50% of CIN II were from the low income group. The present study was also supported by the studies done by Bukhari MH *et al* (2012)[12] who concluded that maximum no of cases were from low SE status.

Age of marriage and duration of exposure to sexual intercourse had a distinct role in genesis of cervical dysplasia. In the present study, the incidence of CIN was 45% and of invasive carcinoma was 86.1% in women who were married at less than 20 years of age which is shown in table VIII. This observation was also supported by Kushtagi *et al* (2002)[8], Sherwani RK *et al* (2007)[13] and MS Bal *et al* (2012)[7] who demonstrated that the severity of underlying CIN increased with increase in the duration of marital life and hence the increase in the duration of exposure to sexual intercourse.

In the present study majority of women complained of excessive white discharge per vaginum (68.3%). Bhojani *et al* (2011)[14] showed in their study that 40.6% cases presented with discharge per vaginum. Excessive vaginal discharge playing a role in contributing to the development of CIN was also proved to be a risk factor in the study conducted by Vaidya *et al* (2003)[9]. In their study, 24% of cases of CIN presented with vaginal discharge.

In the present study post coital bleeding was found in 8.3% cases. Among them CIN was found in 20% of cases, invasive carcinoma in 30% rest 50% had some benign lesion. Shalini R *et al* (1998)[10] in their study showed the relationship of post coital bleeding and CIN. In their study, among the women who had post coital bleeding, 85.5% had benign findings, 5.6% had HPV and CIN I, 3.6% had CIN II and III and 5% had invasive cancer.

In the present study the gross appearances of cervix revealed cervical erosion in 51.7% (62/120) of cases, rest of the cases showed growth in 27.5%, congestion in 10%, Hypertrophy with congestion seen in 5.8%, Hypertrophy with erosion was seen in 13.4% and mucus polyp was found in 4.2% of cases.

CIN was found in 25% (3/12) of women who had congested cervix, in 22.6% (14/62) of women who had cervical erosion, in 42.8 % of women with hypertrophy with congestion and in 25% of women with hypertrophy with erosion. Majority of cases with invasive carcinoma showed growth in the cervix (94.2% cases). This observation was also found by MS Bal (2012)[7] who showed 35.7% cases of erosion in CIN and invasive carcinoma which is consistent with the present study.

In the present study the overall incidence of CIN reported by pap smear was 22.5%. The overall incidence of CIN on cytology was 7.75% reported by Bhojani KR *et al* (2011)[4] and 8.2% by Bukhari *et al* (2012)[12]. In the present study the overall incidence of invasive carcinoma was 22.5%. Incidence of invasive cancer detected on cytology by various studies are 1.75% by Pattnaik & Pati (1987)[14], 0.75% by Bhojani KR *et al* (2011)[4], 2% by Bukhari *et al* (2012)[12].

The disparity between the results of the present study and other studies may be due to selection of high risk cases who had positive symptoms, signs and cervical pathology in the present study where as in most of the other studies mentioned above only mass screening procedures were adapted.

The increased incidence of CIN and malignancy was also due to low literacy rate and low socioeconomic status, lack of health awareness in rural set up along with inaccessibility of proper health care facilities being a cause of neglecting the symptoms in the preclinical stage of cervical cancer.

Sensitivity of pap smear was 86.5% and specificity was 92.18% in the present study. The positive predictive value was 90.7% and the negative predictive value 89.4 %. The accuracy of pap smear was found to be 90% (Table 8).

Table 8: Reference table of Sensitivity and Specificity of Pap smear

S No.	Authors	Sensitivity	Specificity
1	Sankarnarayanan et al (2001)[3]	86%	91%
2	Bhatla N et al (2007)[15]	50%	98.9%
3	Divya Hegde et al (2011)[16]	83%	98%
4	SO Albert et al (2012)[17]	60%	100%
5	Bukhari MH et al (2012)[12]	66%	100%
6	Present study	86.5%	92.18%

This data suggests that the pap smear is less sensitive as a screening tool because it is associated with high false negative results. But in the present study the sensitivity is higher than other studies because the study population in this area present more with invasive disease rather than pre invasive state. Pap smear has higher sensitivity in invasive carcinoma compared to dysplasias. The sensitivity of pap smear can be increased by eliminating high false negative results by proper technique of slide preparation, fixation and reading and when used of pap smear in adjunct to other screening tools like VIA or coloposcopy.

Conclusion

The most common clinical finding in unhealthy cervix & in cervical neoplasia was cervical erosion and for invasive

carcinoma it was cervical growth. Pap smear has high specificity but low sensitivity. The sensitivity of pap smear can be increased by eliminating high false negative results by proper technique of slide preparation, fixation and reading. The increased incidence of CIN and malignancy was due to low literacy rate and low socioeconomic status, lack of health awareness in rural set up, along with inaccessibility of proper health care facilities further compounding the neglect of symptoms in the preclinical stage of cervical cancer. Hence the study concludes that screening programme and awareness regarding cervical cancer should be enhanced and supervised in the grass root level.

Conflict of interest: None

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