

A STUDY OF 80 CASES OF CERVICAL INTRAEPITHELIAL NEOPLASIA IN A DEVELOPING COUNTRY

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SUMMARY

Eighty cases of cervical intraepithelial neoplasia were studied with a view to outline the management in a situation with limited facilities. There were 19 (23.7%) cases of cervical intraepithelial neoplasia Grade II (CIN II) and 61 (76.2%) cases of cervical intraepithelial neoplasia Grade III (CIN III) diagnosed by cytology, colposcopy and histopathology. Papanicolaou cytology was used as a screening procedure in all the 80 cases, while colposcopy was performed in 45 (56.25%) cases. Colposcopy was unsatisfactory in one case where conisation was not done and a pan hysterectomy performed, showed invasive carcinoma. Hence conization is mandatory for cases with unsatisfactory colposcopy. Conization was performed in 37 (46.2%) cases and was therapeutic in 16 (20%) cases. Hysterectomy was performed in 34 (42.5%) cases of CIN III. In 18 (52.9%) of these cases a diagnostic cone had been performed. Radical hysterectomy was performed in 7 (8.7%) cases where cone biopsy showed microinvasive or invasive carcinoma and also where Pap smear showed malignancy although cone histology was CIN III. From this study we feel that Pap smear, colposcopy and conization are mandatory in the evaluation of unhealthy cervix. It is better to resort to a more radical management because of poor compliance of patients for followup due to ignorance, low socio economic status and long distances from hospital.

Introduction

Cytological screening programmes have resulted in the diagnosis of preinva-

sive carcinoma of the cervix and thereby a decrease in the incidence of invasive carcinoma. In addition, the use of colposcopy, target biopsy and conization in the management of CIN have also resulted in a decrease in incidence of CIN and thereby a decrease in radical surgery

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for the same: This study was undertaken to evaluate the role of exfoliative cytology, colposcopy, punch biopsy and conization in the management of CIN in a set up where use of colposcopy is limited and Laser therapy is not available. Consequently the patients who are above the age of 35 years and at risk for invasive carcinoma are advised hysterectomy. However we would like to reiterate the philosophy that conization is an important diagnostic step before proceeding with hysterectomy.

Materials and Methods

At the Gynaecology Outpatient Department of Jawaharlal Institute of Post-graduate Medical Education and Research (JIPMER) Hospital, Pondicherry (Indian), Papanicolaou smears are done for all the patients. Cervical punch biopsy and/or colposcopy directed biopsy are performed when clinical features and cytology are suggestive of cervical neoplasia. A cold knife conization is resorted to whenever CIN III is reported and also in cases of CIN II when the patients are above the age of 35 years and cervix is "unhealthy". From January 1985 through December 1987, 80 cases of CIN II/CIN III were detected. If more than one Pap smear or biopsy was done, only the more severe diagnosis was considered.

Results

A total of 21,600 patients had routine Pap smear and 5,500 had punch biopsy of cervix. Cervical intraepithelial neoplasia (CIN III / CIN II) were detected in 90 cases. There were 19 cases of CIN II of Pap smear/biopsy (random biopsy or colposcope directed) and 61 cases of CIN III. Twenty two cases (27.5%) were seen in the 36-40

years age group and 5 cases (6.25%) in the 31-35 years old. There were 7 (8.75%) in the 19-25 years age group. The women who were married for 20-40 years showed the highest incidence (45%). Maximum number of cases were in the multiparous group who had more than 4 children (45 cases). There was no case in the nulliparous group. Ninety two percent of the cases were encountered in the lower socio-economic group.

The complaints with which the patients presented are depicted in Table I. Vaginal discharge was the main presenting complaint in 55 (68.7%). Some women had more than one complaint. Bleeding disorder were seen in 41 (51.2%), of which irregular bleeding was seen in 14 cases (34.1%), menorrhagia in 11 (26.8%) and postcoital bleeding in 7 cases (17%). There were 9 (21.9%) cases who presented with postmenopausal bleeding. In all the 55 cases with vaginal discharge, hanging drop was studied for *Trichomonas Vaginalis* and was positive in 38 (69%) cases and negative in 17 (30.9%) cases. All these positive cases became negative after treatment with Metronidazole.

The gross lesions seen on the cervix are recorded in Table II. The cervix was eroded in 25 cases (31.25%), hypertrophied in 19 cases (23.75%) irregular in 2 cases (2.5%) and hard in 1 case (1.25%). Growth was seen in 5 (6.25%) cases which is a rare manifestation of CIN.

Table III depicts the cytological findings. It was normal in 14 (17.5%) cases, Squamous cell carcinoma in 3 cases (3.75%), CIN III in 41 cases (51.25%), CIN II in 8 cases (10%) and CIN 1 in 7 cases (8.75%). Hence, 49 cases of CIN II / CIN III were diagnosed by Pap smear.

TABLE I — SYMPTOMATOLOGY STUDIED IN 80 CASES OF CIN III/ CIN II

Symptoms	No	Present
White discharge	55	68.7
Bleeding abnormality	41	51.2
Irregular bleeding	14	34.1
Menorrhagia	11	26.8
Postmenopausal bleeding	9	21.9
Postcoital bleeding	7	17.0
Pain in abdomen	21	26.2
Micellaneous	17	21.25
Backache	5	29.4
Secondary amenorrhoea	4	21.5
Prolapse uterus	3	18.2
Urinary complaints	2	11.8
Itching vulva	1	5.8
Mass vulva	1	5.8
Mass abdomen	1	5.8
No gynaecology complaints	5	6.25

TABLE II — GROSS FINDINGS IN 80 CASES OF CIN III/ CIN II

Findings	No.	Percent
Erosion	25	31.25
Unhealthy cervix	15	18.75
Hypertrophied cervix	19	23.75
Hypertrophy with erosion	2	2.5
Contact bleeding	8	10.0
Growth of cervix	5	6.25
Mucus polyp	4	5.0
Ulcer	3	3.75
Senile vaginitis	3	3.75
Irregular cervix	2	2.5
Hard cervix	1	1.25
Healthy cervix	2	2.25

TABLE III — PAP SMEAR - N = 80 (100%)

	No.	Percent
Negative malignant	14	17.5
Inflammatory smear	6	7.5
CIN I	7	8.75
CIN II	8	10.0
CIN III	41	51.25
Squamous cell carcinoma	3	3.75
Unsatisfactory	1	1.25

Trichomonas vaginalis was positive in 3 smears - two cases of CIN I and one of inflammatory smear.

Random biopsy was done in 39 cases (Table IV) and showed CIN III in 26 cases (66.6%) and squamous cell carcinoma in 2 cases (5.1%) (out of 3 cases on Pap smear). The third case which showed invasive carcinoma on Pap smear, the cervix biopsy showed cervicitis. Hence 30 cases of CIN II (4) and CIN III (26) were diagnosed by random biopsy.

III and 2 cases (4.4%) of CIN II. Abnormal vasculature was associated with one case (1.6%) of CIN III and erosion with 3 cases (4.9%) of CIN III. In 8 cases out of 43 (18.6%) target biopsy agreed with cone biopsy. In 6 cases (13.9%) it was falsely positive. In 3 of these it was CIN III on target biopsy and study of cone biopsy was cervicitis. In the other 3 it was CIN I

TABLE IV — RESULTS OF RANDOM BIOPSY (N = 39)

	No	Percent
Cervicitis	6	15.3
CIN I	1	2.6
CIN II	4	10.2
CIN III	26	66.6
Squamous cell carcinoma	2	5.1

TABLE V — COLPOSCOPIC FINDING IN 45 CASES

	Normal	Punctuation	Mosaic	White Epithelium	Abnormal vessels	Unsatis factory	Erosion
CIN I	-	2		2			
CIN II	-	6	2	5			
CIN III	1	8	7	14	1	1	3
Metaplasia		1		1			
Cervicitis		1		2			
Squamous cell carcinoma.							

Colposcopy was carried out in 45 cases (56.25%) and directed biopsy in 43 cases (95.5%). The results are shown in Table V. White epithelium was the commonest colposcopy finding seen in 24 cases (53.3%). Amongst these were 14 cases (31.1%) of CIN III and 5 cases (11.1%) of CIN II. Punctuation was seen in 8 cases (17.7%) of CIN III and 6 cases (13.3%) of CIN II. Mosaic was seen in 7 cases (15.5%) of CIN

on cone. Two cases of CIN III on target biopsy were microinvasive carcinoma on cone. Hence, false negative rate was 4.5%.

Conization was performed in 37 (46.2%) cases and was therapeutic in 16 (20%) cases. The cone specimen showed CIN III in all the 15 cases in the age group 25-34 years with disease free margin of resection. Follow up was normal in all of them.

Hysterectomy was performed in 34 (42.5%) cases of CIN III who were above 35 years of age. In 18 (52.9%) cases a preliminary cone was performed and 10 cases with CIN III on cone biopsy the final hysterectomy specimen showed cervicitis. In 5 cases the biopsy agreed with hysterectomy histology (CIN III). Therefore, the cone histology was more advanced than that of hysterectomy in 10 cases. Probably, the cone had completely excised the abnormal lesion. Colposcopic evaluation had been done in 20 cases prior to conization and cure rate was found to be higher. In one case conization showed CIN III while hysterectomy specimen showed microinvasive carcinoma. While in other, microinvasive carcinoma on cone turned out to be invasive carcinoma in hysterectomy histology.

Out of 19 cases of CIN II, cryosurgery was performed in 9 (47.3%) cases after colposcopic evaluation. Only 6 cases reported for follow up. In 4 of the 19 cases (21%) of CIN II conization was performed and it revealed more advanced lesion (CIN III in 2 cases) and cervicitis in 2 cases. Hence the conviction that conization is necessary in CIN II when patients fall in the risk group.

Hence, residual lesion was seen in 9 of the 18 cases where hysterectomy was performed after conization for CIN III. In 5 cases CIN III lesion persisted. Radical hysterectomy was performed in 7 patients belonging to the 32-45 years age group. All were parous women. Only in 2 case prior conization was performed. These cases had CIN III on Pap smear and colposcopy showed erosion and punctation respectively. Conization revealed CIN

III in one and microinvasive carcinoma in the other. Hence conization is of great importance for diagnosing invasion before proceeding with radical hysterectomy. In the other 5 cases, where Wertheim's hysterectomy was performed without prior cone, squamous cell carcinoma was reported in the biopsy/Pap smear in 3 cases. There was a frank growth in one case and atypical vessels on colposcopy in the other. The final diagnosis in all cases was CIN III.

Discussion

In the current study CIN III was seen most often in the 36-40 years age group. 92% of the women belonged to the low socioeconomic group and were of high parity. This explains the various epidemiological factors associated with cancer cervix.

White discharge, irregular bleeding and contact bleeding were the most ominous symptoms. Five cases had no symptoms pointing to cervical neoplasia hence the importance of routine Pap smear in all sexually active women. Erosion of cervix was seen in 25 cases. Therefore thorough evaluation of any abnormal lesion of cervix by Pap smear and colposcopy is required before conservative treatment.

Pap smear was done in all 80 cases. In all the 55 cases with vaginal discharge a hanging drop was studied for *Trichomonas vaginalis*. It was positive in 38 (69%) cases and negative in 17 (30.9%) cases. *Trichomonas vaginitis* mimicks early cancer on Pap smear and colposcopy. It may give rise to contact bleeding which is also a symptom of carcinoma cervix. Patients with chronic *Trichomonas vag-*

initis are at high risk for carcinoma cervix. Treatment of infection is necessary before ruling out a dysplastic smear.

Colposcopy in 45 cases showed mosaic, punctation and white epithelium as the common findings associated with CIN II and CIN III. However, abnormal vessels though a feature of invasive carcinoma was seen in one case and erosion cervix in 3 cases. In 18.6% cases the target biopsy agreed with cone biopsy. In 14.2% cases it was false positive and in 4.5% cases it was false negative. Cytology and colposcopy are complementary methods in the diagnosis of CIN. The accuracy of cytology alone in the detection of CIN III is 88.9% and colposcopy alone is 90-97.7% and both employed together it is 80-90% (Limited 1958; Stafl and Mattingly 1973). The false negative rate of colposcopy is 3.3% and that of its directed biopsy is 0.3% (Stafl and Mattingly 1973). When the upper limit of Transformation zone is fully visible the final histology is accurate in 99.3%.

The histology of cone specimen agreed with directed biopsy (CIN III) and cone margins were free of disease in 16 cases. In these cases conization was therapeutic. In 34 cases of CIN III hysterectomy was performed of which 18 cases were preceded by a diagnostic cone. Residual lesion of CIN III persisted in 5 cases. In two cases the hysterectomy specimen showed a higher lesion. Rajaram (1970) in his study of 25 cases where cone Biopsy was performed for abnormal cytology and/or cervical Biopsy Histology, found it a useful procedure to rule out invasive carcinoma.

In a similar study by Selim (1973), a total of 168 patients had cervical biopsy. Thirty two had simple or radical hysterectomy depending on diagnosis from punch biopsy and hysterectomy performed 6 weeks later showed residual lesion in 18 cases.

Conservative measures like cryosurgery, electrocautery and laser have now presently emerged as treatment for CIN II and CIN III after full colposcopic evaluation. In the current study no patient with CIN III had such therapy due to non-availability of laser and unreliability for followup. Nine patients with CIN II had cryosurgery and 6 cases came for follow up. In 4 cases of CIN II cone was performed and revealed more advanced lesions in 2 cases (CIN III) where a final hysterectomy specimen showed only cervicitis. 3 cases with CIN II had ward mayo's operation for uterovaginal prolapse and showed CIN III in the final specimen of only 1 case. Kaufman and Irwin (1978) in the treatment and follow up of 395 women with CIN III found residual atypia in 44 (77%) within 12 months of cryosurgery.

In our series no case of conization as therapeutic procedure had an abnormal Pap smear on follow up upto 3 months. The same was noted for hysterectomy (Simple/redical) done for CIN III. Due to low compliance of patient followup we have employed hysterectomy in all patients above 35 years who had completed their family and showed CIN III on conization.

Some authors have condemned hysterectomy as a modality of treatment for

CIN III Kreigar and McCormack (1963) reported a failure rate of 9.1% for cone in his study of 414 patients with CIN III. He advocated hysterectomy only in patients with persistent abnormal smear. Bjerree et al (1976) advocated conization as the treatment of choice for CIN III. Curative rate (87%0 depended on freedom of disease from resection margins. (A finding also noted by Ahlgren (1975) who reported 98% cure rate when cone margin were free of disease and 70% when the margins were involved.

Conclusions

From this study of the 21600 cases screened by Papanicaloau smear 80 cases of CIN I/CIN III were detected in the year 1985-1987. Therefore a routine Papanicaloau smear must be carried out on all women attending the gynaecology out patient department.

(2) Colposcopy, target biopsy and conization further helped evaluation of the cases with abnormal smear and grossly suspicious cervix. Colposcopy was useful in delineating the abnormal zone for target biopsy and the margin of resection of cone.

(3) Conization was an important diagnostic aid for cases with CIN II/CIN III. It helped to rule out invasion and was therapeutic in young women.

(4) Hysterectomy was reserved for older women above 35 years who had completed their family and conization specimen showed CIN III or CIN II. This was decided due to the poor compliance of patients for follow up.

(5) For CIN II after through colposcopy, cryosurgery was performed.

(6) Whenever colposcopy is unsatisfactory a conization is a must before resorting to hysterectomy, to rule out an invasive carcinoma. We came across an invasive lesion in the simple hysterectomy specimen of a case where colposcopy was unsatisfactory and conization was not done prior to hysterectomy. In such a case a Wertheim's hysterectomy could have given better cure rate had conization been performed.

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References

1. Ahlgren M, Inegmarss on I, Lindberg L, Nordqvist B. *Obstet. Gynecol.*, 46: 135, 1975.
2. Bjerre B, Eliason G, Linell F, Soderberg H, Sjoberg. *cervix. Am. J. Obstet. Gynecol.*, 125: 143, 1976.
3. Kaufman R.H; Irwin JF. *Am. J. Obstet. Gynec.*, 131; 381. 1978.
4. Kreigar JA, McCormack L.J, Bradley, V F — *Am. J. Obstet. Gynec.*, 86: 120, 1963.
5. Limberg H. *Am. J. Obstet. Gynec.* 75: 1298, 1958.
6. Rajaram P.Santpur S.R.Rao C.M. *Compose; Achives Vol 1: No.1 & 2 June - Dec. 1970.*
7. Selim MA, Sobosita L.J, Blair OM, Little BA. *Obstet. Gynec.* 41: 177, 1973.
8. Stafl A, Mettingly R.F. *Obstet. Gyne.* 41: 168, 1973.