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Clinical, Investigative, Postoperative Status in Cervical Precancer and Cancer

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Abstract

Early diagnosis and accurate staging are essential for appropriate management of cervical cancer, one of the most common cancers and leading cause of cancer deaths worldwide. The objective of present study was to know the correlation between clinical, investigative, surgical and histopathological diagnosis in suspicious and staging in obvious cancer cases. Study subjects were of 20-64 years, diagnosed over 2 years with aid of visual inspection (VI), vaginal and cervical cytology, visual inspection after application of acetic acid (VIA), VI after application of Lugol's iodine (VILI), followed by colposcope guided cervical biopsy, intraoperative and postoperative staging after histopathology of specimen in clinically suspicious and obvious cancer cases. Of 100 clinically suspicious cancer cases, 10 (27.0%) out of 37 women of 20-40 years (five stage IA and five stage IIA), 14 (22.2%) of 63 women above 40 years (one stage 0, four stage IA and nine stage IIA) were proved cancers after investigations, a total of 24%. Of 78 obvious cancer cases upto stage IIA, 28 (35.9%) were clinically stage IA, 15 (53.5%) remained IA, nine turned out to be IIA, two IB and two were IIIA. Of 29 clinical stage IB, 18 (62.1%) were confirmed IB, three were IIA and eight were IIIA. Of 21 clinical IIA, only seven (30.4%) remained IIA and 14 turned out to be IIIA after investigations. Seventy underwent therapeutic surgery. Staging after radical hysterectomy was stage 0 in one (1.4%), IA in 18 (25.7%), IB 19 (27.1%), IIA in 25 (35.7%), IIB one (1.4%), IIIA five (7.1%) and one was a case of mixed malignant mullerian tumor. Finally of 102 cervical cancer cases (clinically obvious 78 and suspicious confirmed 24 upto stage IIA), one was confirmed stage 0, 18 stage IA, 19 stage IB, 24 IIA, one IIB, 33 IIIA, and one mixed malignant mullerian tumor (excluding the five lost to follow up). It was revealed that VI, cervical/vaginal cytology, VIA, VILI colposcopy cervical and vaginal biopsies, not only help in diagnosis in suspicious cases but also in assessing vaginal extent of the disease, and planning right therapy including adjuvant therapy.

Keywords

Clinical staging; Investigative modalities; Surgical-histo pathological staging

Background

Each year more than 500,000 women are diagnosed with invasive cervical cancer, and close to 275,000 women die of cervical cancer worldwide, making it the third most common cancer and fourth leading cause of mortality among women. More than 85% of cervical cancer related deaths occur in developing countries, where screening programmes are not readily available though cervical carcinoma is the leading cause of cancer related deaths among young women [1]. Detection of the precancer, early stage cervical cancer leads to uncomplicated therapies essential for quality life. Once diagnosis is confirmed, next step is to know the status, extent of the disease for staging, the key factor in selecting the right treatment [2]. FIGO (International Federation of Gynaecology and Obstetrics) staging of cervical cancer is based on careful clinical examination, if necessary under anaesthesia [3,4] and remains the primary modality for planning [5,6]. However final histopathology provides exact status, type and extent of disease and is the basis for the therapy even after surgery [7].

Objective

To study the relationship between clinical, investigative, surgical and histopathological diagnosis in suspicious and obvious cases of cervical cancer by analyzing findings of histopathology in all the cases subjected to biopsy and therapeutic surgery.

Material and Methods

The present study was carried out in obstetrics and gynaecology department of a referral rural hospital over a period of two years after approval of ethical committee. The women who had suspicious cervical precancer/cancer and obvious cancer were studied and the clinical, investigative, surgical, histopathological diagnosis and staging were correlated.

Women admitted as suspicious and obvious operable cases of cervical cancer up to stage IIA of 20-64 years with no previous surgery on cervix, either having abnormal vascularity or follicular erosion which bled on touch or ulcer, or obvious disease (exophytic condylomatous, cauliflower, polypoidal or infiltrating) over the cervix, were included in the study. Further evaluation was done for confirmation of diagnosis, staging to plan management which was executed.

Procedures included visual inspection (VI), followed by vaginal/cervical cytology, visual inspection after acetic acid (VIA) applied to cervix and upper vagina and followed by VI with Lugol's iodine (VILI). Inspection was followed by colposcopy, cervical vaginal biopsies and intraoperative and postoperative staging by histopathology of surgical specimen.

Over the study period 22,524 women attended gynaecology outpatient and 2,295 (10.2%) got admitted, of which 241 (10.5%) were clinically obvious cancer, 28 (11.6%) stage IA, 29 (12%) IB, 21 (8.7%) IIA, 46(19%) IIB, 33 (13.7%) IIIA, 33 (13.7%) IIIB, 30 (12.4%) IVA and 21 (8.7%) IVB. So 78 (32.4%) up to stage IIA were included as per the inclusion criteria, 16 (20.5%) 20-39 years, 62 (79.5%) above 40 years. Additional 200 (8.7%) were suspicious of precancer/cervical cancer, but 38 (16%) did not fulfil the inclusion criteria of the study, 43 (21.5%) didn't give consent, 19 (9.5%) were dropouts and hence 100 (50%) suspicious cases were included.

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Results

Of 100 suspicious cases 37 were of 20-40 years, 63 above 40 years, one was confirmed stage 0 and 23 were confirmed staged up to IIA, total of 24, [10 (41.7%) between 20-40 years, 14 (58.3%) above 40 years]. After the investigations these 24 underwent surgery, 23 radical (Tables 1 and 2).

Seventy eight clinically staged cases had restaging after investigations, surgery and operative specimen histopathology. Thus total study subjects were 102 (78 of 241 obvious cancer and 24 confirmed cancer cases out of 100 suspicious), 26 (25.5%) of 20-40 years, 76 (74.5%) above 40 years. Of the 26 cases between 20-40 years, (10 out of clinically suspicious and 16 of clinically obvious (two IA, ten 1B and four IIA), 18 (69.2%) (six IA, four IB and eight IIA) had same stage on final evaluation after VIA, VILI, colposcopy of cervix and vagina, cervical and vaginal cytology as well as histopathology after radical hysterectomy, however, eight (28.6%) were not so, one IA and one IIA were staged IIIA after VIA, VILI, colposcopy of cervix and vagina, cervical and vaginal cytology and six clinical stage IB, on investigations and surgery were having stage IIIA, confirmed histopathologically. Of the 76 women above 40 years (14 clinically suspicious and 62 obvious cancer; 26 IA, 19 IB and 17 IIA), on investigations, was stage 0 (1.3%), 19 (25%) stage IA, 14 (18.4%) IB, 19 (25%) IIA and 18 (23.7%) were IIIA, five IA were lost to follow up during work up. So of 76 cases above 40 years 23 got excluded at this stage and 53 (63.6%) up to IIA were planned for radical hysterectomy, one stage IIA died before surgery due to myocardial infarction and so 52 underwent hysterectomy (one stage 0, 19 IA, 14 IB and 18 IIA), 51 radical hysterectomy. One stage 0, 13 of 13 IA continued same stage, 14 continued IB and 3 remained IIA but one stage IA was IB, one stage IA was staged IIB and 5 IIA were IIIB intra-operatively. After histopathology of surgical specimens, one was finally confirmed stage 0, 12 were stage IA, 15 IB, 16 IIA, one IIB, seven IIIA and one turned out to be mixed mullerian malignant tumor (MMMT) (Tables 1 and 2).

Discussion

Status and stage of the disease are the key factors in selecting the right treatment and prognosis in cervical cancer. Adequate visualization and palpation of the cervix, vagina and fornices help in assessment **of** the **local** spread. **T**he disease and its extension **o**n the cervix and vagina may be apparent or the infiltration may be sub-epithelial and suspected only on the basis of obliteration of the vaginal fornices or the presence of apical stenosis or by investigative procedures [8]. Screening programs for the diagnosis of precancer and cancer have been used in decreasing the incidence and mortality from cervical cancer in the developed world [9]. Sankaranarayanan et al. [8] had reported VIA and cervical cytology, both having similar performance in detecting CIN II or more severe lesions and Basu et al. [10] later reported the sensitivity of VIA and cytology in detecting CIN II or worse disease as 88.6% and 81.9% and specificity 78.0%, 87.8% respectively and the sensitivity of VILI to detect CIN II or worse disease, 87.2%, and specificity, 84.7%. Sankaranarayanan et al. [11] also report that VIA is an effective method of reducing the incidence and mortality from cervical cancer in developing countries. Up to seven years of follow-up, the incidence of cervical cancer was reduced by 25% among women who lived in areas where VI was offered and mortality from the disease was reduced by 35%, compared with the incidence and mortality in areas without screening.

A study from Zimbabwe revealed the sensitivity of VIA and cervical cytology for high grade squamous intraepithelial lesions as

Table 1: Clinical, Investigative and Surgical Correlation in Clinically Obvious Cancer.

Staging Age (Years)	Clinical staging	Investigative Staging	Surgical Staging	Final Post HP of Cx and Vag B in inoperable and post operative specimens in Radical Hysterectomy	Total (78)
20-40	2 IA 10 IB 4 IIA	1IA 4 IB 3 IIA 8 IIIA	1 I A 4 IB 3 IIA	1 IA 4 IB 3 IIA 8 IIIA	16
>40	26 IA 19 IB 17 IIA	15 IA (5 lost) 14 IB 10 IIA 18 IIIA	8 IA 15 IB 9 IIA* 1 IIB 5 IIIA	8 IA 15 IB 9 IIA 1 IIB 23 IIIA 1 MMMT	62

*= One patient of stage IIA died before surgery.
MMMT= Malignant Mixed Mullerian Tumor
HP= Histopathology, Cx= Cervix, Vag= Vagina, B= Biopsy
78 cases upto stage IIA underwent radical hysterectmy

Table 2: Clinical, Investigative and Surgical Correlation in Clinically Suspicious cases.

Staging	Clinical suspicious cases			Investigative Staging	Surgical Staging	Final Post HPS of Cx and Vag B in inoperable and post operative specimens in Radical Hysterectomy	Total
Age (Years)	Cervicitis	Cervical Intraepithelial Neoplasia	Total				
20-40	16	11	27	5 1A 5 IIA	5 IA 5 IIA	5 IA 5 IIA	37
>40	41	8	49	1 Stage 0 4 IA 9 IIA	1 Stage 0 4 IA 8 IIA 1 IIIA	1 Stage 0 4 IA 7 IIA 2 IIIA*	63
Total	57	19	76	24	24	24	100

HPS= Histopathology Stagging, Cx= Cervix, Vag= Vagina, B= Biopsy

76.7%, 44.3% and the specificity 64.1% and 90.6% respectively [12]. Perkins et al. [13] have conducted a study in 1,709 women who either had VIA and Pap's test or Pap's test alone. Once the disease is confirmed, final histopathology of the surgical specimen continues to provide information that is central to final treatment planning and prognosis for an individual patient. Whitney et al. [14] reports that in their study of 1,127 patients with stage IB cervical cancer, 98 (8.7%) were found to have extra uterine disease at operation and the proposed radical operation had to be abandoned. In the present study when visual, palpatory and investigative staging were correlated, of 102 cases (24 out of 100 clinically suspicious later confirmed cases and 78 clinically obvious cancer cases up to stage IIA), 70 (24 of suspicious confirmed and 46 clinically obvious) underwent therapeutic surgery (one stage 0, 20 stage I A, 18 stage IB and 31 stage IIA). On correlating clinical and intra-operative staging, one was stage 0, of 20 clinical stages IA, 18 (90%) were stage IA intraoperatively also, but one turned out to be IB (5%) and one was IIB (5%). All 18 women with clinical stage IB had same stage intraoperatively. Of 31 clinical stages IIA, intra-operative staging was IIA in 25 (80.6%); IIIB in five (16.1%) cases and one was MMMT.

Overall correlating investigative staging with histopathological staging of 102 (78 obvious and 24 suspicious confirmed) cases, in obvious cancer of 28 staged clinically IA, 16 (57.1%) were confirmed to be having the same stage after investigations and one was IB, one IIB five were IIIB however five stage IA patients were lost before surgery. Of 29 (37.1%) of stage IB, 17 (58.6%) remained same stage and 12 were IIIA. Of 21 (26.9%) staged IIA, 18 (85.7%) were confirmed IIA, two were stage IIIA and one MMMT. All 18 (23.1%) staged IIIA on visual investigations were found to be the same on histopathological examination after vaginal biopsies also. Out of 24 suspicious cases, one stage 0 remained 0, all 9 stages IA were found to be of same stage intraoperatively. Of 14 stage IIA on investigations 13 (92.9%) were of same stage but one was found to be stage IIIB intraoperatively.

Visual methods continue to be used in diagnosis of cervical pathology though they cannot be relied upon completely because of low specificity. However cervical, vaginal cytology, VIA, VILI and cervical, vaginal colposcopy can also be used to assess vaginal spread of the disease. Parametrial spread can be known only during surgery and histopathology of the specimen and left over edges even if suspicious with high tech imaging which as such is not available to poor who are the ones to get cervical cancer. So VI, cervical and vaginal cytology, VIA, VILI and colposcopy guided cervical and vaginal biopsies, are useful not only in diagnosis but also in assessing vaginal extent of the disease, along with the clinical evaluation for better outcome. Investigative, intraoperative and histopathological diagnosis is complementary in making the diagnosis and spread for best of therapy and outcome.

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