

Significance of inflammation in cervical cytology smears in rural women of India: An observational study

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Abstract

Introduction: Inflammatory smears are frequently seen in cervical cancer screening and they have been widely implicated as precursor of premalignancy of cervix. In the present study, attempt has been made to find out correlation between inflammation and different predisposing factors to cervical carcinogenesis in the rural context.

Materials and Methods: Cervical cancer screening is in progress in the rural population of West Lucknow, India since May 2013 under the auspices of Era's Lucknow Medical College and Hospital, Lucknow, India and till March 2018, cervical smears of 2563 women have been cytologically examined.

Results: The incidence of inflammation was found to be 33.7% in the present series. It was non-specific in 91.3% and was associated with either *Candida albicans* or *Trichomonas vaginalis* in 8.2% of cases. The inflammation was associated with low grade squamous intraepithelial lesions of cervix (LSIL) in 176 cases (20.1%) which were mostly asymptomatic (36.1%) and some had cervical lesions on the cervix (11.2%). The inflammatory smears were mostly seen in women complaining of vaginal discharge (47.1%) or vague pain in the lower abdomen (31.9%). The inflammation was more common in younger sexually active women between 21-40 years and was seen rising with increasing parity.

Conclusion: The accumulated data points out that the clinical lesions of cervix and multiparity have some impact in the initiation of inflammatory changes in the cervical epithelium. The inflammatory smears, whenever, reported should be adequately treated and smears are repeated after 6 months to rule out any persistence of inflammation or development of any premalignancy.

Keywords: Inflammation, LSIL, STDs, Rural women.

Introduction

Inflammatory changes in the cervical epithelium are commonly encountered during routine cervical cancer screening. In some, the inflammation is associated with the presence of some microorganism while in others, it is non-specific. This poses great problem to the gynaecologist for delineating the line of treatment and usually anti-inflammatory regimen is recommended to the patients with request to come for repeat Pap smear after 6 months to see whether the inflammation is eliminated or is still persisting. The persistence of inflammation is cause of great concern and colposcopic evaluation of cervix is mandatory to find out any pre-malignant changes originating from the inflammation. It is obvious because the inflammatory changes have been presumed to be the precursors of premalignancy of cervix. The earlier studies have demonstrated a strong relationship between persistent inflammatory smears and high percentage of cervical intraepithelial neoplasia (CIN), Human Pappiloma Virus (HPV) and even carcinoma cervix.¹

Single life time cytological screening is in progress since May 2013 in rural areas of West Lucknow under auspices of Era's Lucknow Medical College and Hospital, Lucknow, India and till March 2018, cervical smears in a total of 2563 women have been cytologically examined. Since sufficient number of inflammatory smears has been encountered in these

women, we thought it interesting to investigate their relationship with different predisposing factors to the cervical carcinogenesis such as age, parity, clinical lesions of the cervix, gynaecological symptoms and different sexually transmitted diseases (STDs). This will provide valuable information for discriminating high risk cases in which follow-up could be planned in future to find out whether the inflammatory lesion is still persisting or has reverted back to normal after treatment.

Materials and Methods

The cases for the present study have been collected during ongoing rural cervical cancer screening program in Kakori and Malihabad blocks of West Lucknow, India. Till now, a total of 2563 women have been registered (May 2013- March 2018). Prior to starting the screening, ethical clearance was obtained from the Ethical Committee of Era's Lucknow Medical College and Hospital, Lucknow. The study is being carried out through organizing camps in the villages after proper motivation and door-to-door counseling and distribution of informative literature to women of the villages. At the camp, after taking informed consent, the cervical smears of the women were collected by the gynaecologist who was assisted by a trained nurse. The women who have undergone hysterectomy and who were pregnant were excluded from the study.

The cervical smears were stained according to Papanicolaou's technique and the cytopathological changes observed were graded according to revised Bethesda system of classification. The criteria for diagnosis of inflammation in the cervical smear were cellular changes seen in the squamous cells. The changes seen in the nucleus are nuclear enlargement and loss of chromatin pattern resulting in the diffuse pattern of the chromatin (Fig. 1). The changes in the cytoplasm includes vacuolization in the cytoplasm depending upon the severity of inflammation and many large and small vacuoles may be seen (Fig. 2). Often perinuclear halo formation (Fig. 3) and binucleation are visible (Fig. 4).

All the collected data has been statistically analyzed using Chi-square test, MS EXCEL.

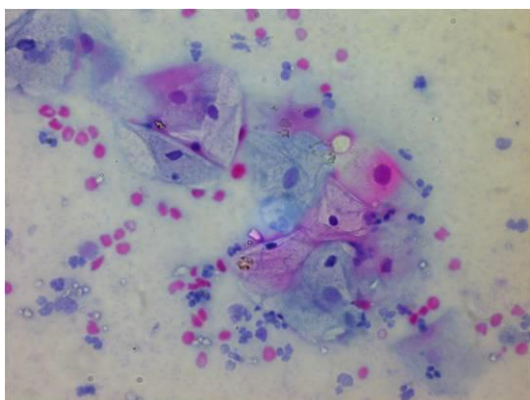


Fig. 1

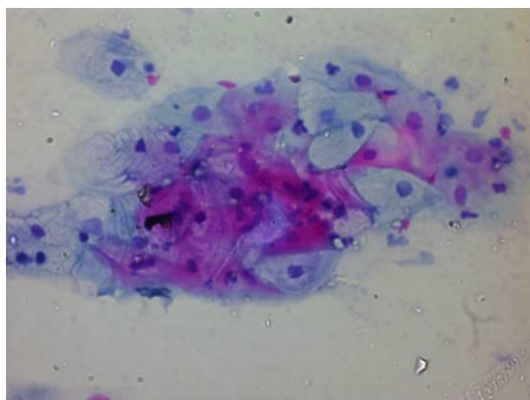


Fig. 2

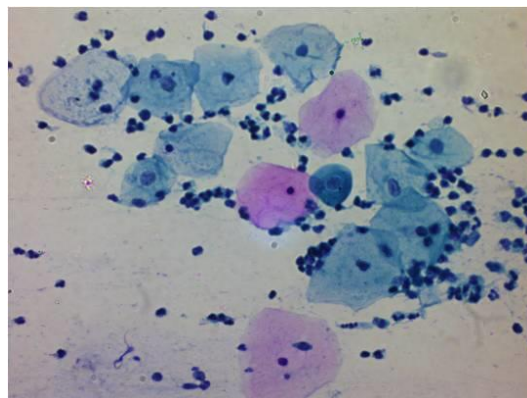


Fig. 3

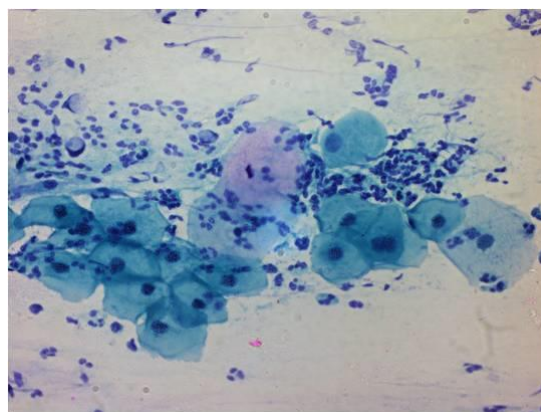


Fig. 4

Results

The incidence of inflammatory smears in the total 2563 rural women was found to be 33.7% (864 cases). The inflammation was seen in symptomatic women in 678 out of 1721 cases (39.3%) while in asymptomatic group, the incidence was 22.1% (186/842 cases). The inflammatory changes in the cervix were thus higher with symptoms (39.3%) than without symptoms (22.1%) and the difference was statistically significant ($\chi^2=52.78$; $p<0.001$).

The inflammation was associated with low grade intraepithelial lesions of cervix (LSIL) in 20.3% of cases (176/864). The distribution of these 176 LSIL cases in symptomatic and asymptomatic women was found to be as follows:

1. Symptomatic group: LSIL- 109/678 cases (16.1%).
2. Asymptomatic cases: LSIL- 67/186 cases (36.1%).

The difference in the LSIL incidence between the two groups was found to be significant. ($\chi^2=19.48$; $p<0.001$). A high incidence of LSIL in women without symptoms shows that progression of SIL from the inflammatory lesions of cervix has no relation with the onset of gynaecological symptoms. It appears that the clinical lesions of cervix are largely associated with initiation of inflammatory and SIL changes in the cervix. In fact, clinical lesions were present in the cervix in 17.1% (148 cases) out of total 864 cases. Of

these, 15.5% were seen in the symptomatic women as against 22.1% in the asymptomatic group. The inflammation was mostly associated with erosion cervix (11.2%). Different types of clinical lesions of cervix between the two groups are shown in Table 1. The statistical analysis revealed insignificant difference in the asymptomatic and symptomatic women as regards occurrence of different clinical lesions of cervix.

On the whole, the inflammation was found to be non-specific in 91.7% of cases (793/864) while this was associated with presence of micro-organism in 8.2% of the cases (71/864). Individually, in symptomatic women, the non-specific inflammation was 91.4% (613/678) while this was 96.7% (180/186) in asymptomatic group. Similarly, the percentage of Inflammatory smears associated with micro-organism was low (3.2%) in asymptomatic women than 11.5% observed in the symptomatic group. Two micro-organisms namely *Candida albicans* and *Trichomonas vaginalis* were seen in the inflammatory smears and their incidence in the symptomatic and asymptomatic women are shown in Table 2. There was no statistically significant difference in the incidence of *Candida albicans* and trichomonal infection in the two groups. It appears that the inflammatory smears were mostly associated with Candidiasis (5.3% - 50 out of 864).

In the symptomatic women, 3 types of gynecological symptoms were mainly seen viz. vaginal discharge, vague pain in lower abdomen and different

types of menstrual disorders mainly irregular menses Table 3. The inflammatory smears are most commonly associated with vaginal discharge (47.1%) followed by pain in lower abdomen (31.9%). The inflammatory changes were less common with menstrual irregularities (11.9%).

The incidence of Inflammation was also analyzed in relation to age in 864 women (Table 4). The incidence was found maximum in the young sexually active women between 21- 30 years (47.5%) followed by 31-40 years age group (38.3%). In fact, 86.7% (746 out of 864) of women in the study group belonged to 21-40 years age group. The incidence was almost identical in different age groups in symptomatic and asymptomatic women and there was no significant difference in the incidence in different age groups ($\chi^2=10.1$; $p=0.018$).

As regards parity, the analysis revealed a rising trend of inflammatory smears with increasing parity (Table 5) and the incidence was very high with multiparity (68.1%). It appears that the multiparity has some bearing on the initiation of inflammatory changes in the cervix. The incidence of inflammation was almost identical with different parities in both symptomatic and asymptomatic group of women and there was no statistical significant difference in the incidence of two age groups.

Table 1: Inflammation incidence with different types of clinical lesions of cervix

Clinical lesions of cervix	Total number of cases (864)	Symptomatic women (678)	Asymptomatic women (186)
Erosion cervix	97 (11.2%)	74 (10.9%)	23 (12.2%)
Hypertrophied cervix	30 (3.4%)	20 (2.9%)	10 (3.3%)
Cervix bleeds on touch	4 (0.4%)	2 (0.3%)	2 (1.07%)
Others (Cervicitis, Endocervical polyp, Cystocoele and Rectocoele)	17 (1.9%)	8 (1.1%)	9 (4.8%)

Clinical lesions present – 17.1% (148 /864)

Table 2: Incidence of inflammation in relation to different STDs

Type of STD	Symptomatic women (678)	Asymptomatic women (186)	Total (864)
<i>Candida albicans</i>	45 (6.6%)	5 (4.6%)	50 (5.7%)
<i>Trichomonas vaginalis</i>	20 (2.9%)	1 (0.5%)	21 (2.4%)

Non-specific – 91.7% (793/854)

Associated with presence of micro-organism – 8.2% (71/864)

Table 3: Incidence of inflammation in relation to different gynaecological symptoms

Gynaecological symptoms	Total number of cases showing Inflammation	Incidence
Vaginal discharge	409	47.1%
Vague pain in lower abdomen	278	31.9%
Menstrual disorders	104	11.9%

Table 4: Incidence of inflammation in relation to age

Age groups	Total number of cases (864 cases)	Symptomatic women (678 cases)	Asymptomatic women (186 cases)
<20 years	45 (5.2%)	36 (5.3%)	9 (4.8%)
21-30 years	413 (47.8%)	331 (48.8%)	82 (44.1%)
31-40 years	328 (37.9%)	249 (36.7%)	79 (44.4%)
> 40 years	78 (9.1%)	62 (9.1%)	16 (8.6%)

Table 5: Incidence of inflammation in relation to parity

Parity groups	Total number of cases (864 cases)	Symptomatic women (678 cases)	Asymptomatic women (186 cases)
Nulliparous	67 (7.7%)	43 (6.3%)	24 (12.9%)
P1	66 (7.6%)	50 (7.3%)	16 (8.6%)
P2	151 (17.4%)	115 (16.9%)	36 (19.3%)
P3 and above	580 (67.1%)	470 (69.3%)	110 (59.1%)

Discussion

The incidence of inflammatory smears was found to be 33.7% in the present series, Bhutia, et al have also found a low incidence of 20.3% of inflammation in their series.²

Misra et al in a Hospital based cytological screening in urban women of Lucknow have reported inflammation to the tune of 49.6%.³ However, some investigators have reported very high incidence of inflammation in their Pap smear studies (Diagloglu et al. - 65.5% and Barouti et al. - 77.2%).^{4,5} An association was also found with LSIL changes and inflammation in 19.8% of cases in the present series. Dasari, et al have also seen LSIL in 20.9% and HPV infection in 17% of women showing persistence of inflammation who were subjected to colposcopic biopsy.⁶ Bhutia, et al has also found similar results - 16.6% of CIN in their study. Achour et al. have observed in the histology of biopsies taken in women showing persistence of inflammation that 24.7% of cases had CIN along with 1 case of squamous cell carcinoma. In the present series, SIL changes were associated with inflammation in high percentage of asymptomatic women (36.1%) as against 16.1% in the symptomatic group. It appears that symptoms have little impact on the production of inflammation in the cervix.

Inflammation was found to be non-specific in 91.7% of cases in the present series while in the remaining 8.2% of cases it was associated with the presence of some micro-organism. Dasari et al. have also reported non-specific inflammation in the 92% of cases. However, Roeters et al. have found a low incidence of non-specific inflammatory changes to the tune of 66.4% in their series.⁷

In the present study, only two micro-organisms namely *Candida albicans* and *Trichomonas vaginalis* have been investigated in rural women. Their incidence was found to be 6.6% and 2.9% respectively. Both these micro-organisms as expected were higher in the symptomatic group than without symptoms Baka, S et

al. have found almost 60% of women presenting inflammatory smears on the cervical smear examination had positive cultures for different pathogens.⁸ They opined that cervicovaginal microbial flora characterization is necessary and treatment of the inflammation will be facilitated by the specific treatment of the micro-organism diagnosed on the inflammatory smears. Burke et al have also demonstrated that the prevalence of infection was higher in the inflammatory smear group indicating that the women with inflammatory smears are more likely to harbor genital tract infection than with women with no evidence of inflammation on cytology.⁹

A comparatively high incidence of *Candida* has been reported by many authors. Barouti et al. have reported 10.6% of *Candida* in the inflammatory smears, and have suggested that the presence of inflammation was significantly associated with vaginal candidiasis Burke et al have also reported 11.6% *Candidal* infection in women with inflammatory smears.

The low prevalence of *T. Vaginalis* as reported in the present series was also found by Burke et al. and Barouti et al. Similar reports have also been demonstrated by Depuydt et al. by using real time PCR.¹⁰ However, Madhivanan et al. have found 8.3% of *T.V* infection in Indian women.

Inflammation was more evident in the present series in the younger sexually active women between 21-40 years of age irrespective of whether symptom was present or not.¹¹ The inflammatory changes were low in the postmenopausal women. Dasari et al. has reported mean age of inflammation as 37 years. The inflammation showed rise with parity in the present series while Dasari et al. have found mean parity of 2.6 in their series of women showing inflammatory smears it appears that the high parity plays some role in the initiation of inflammatory changes of the cervix.

In symptomatic women, the inflammatory smears were commonly associated with vaginal discharge (47.1%) followed by vague pain in the lower abdomen

(31.9%). Dasari et al. have also reported similar findings. In the present series, the inflammatory smears were mostly associated with cervical erosion in both symptomatic and asymptomatic women (10.9% as against 12.3%). Dasari et al. have found 20% of women with the inflammatory smears presented erosion cervix on clinical examination. However, the study has some limitations as it is very difficult to get the women for repeat smears to see persistence of the inflammation, if any and also for taking swab for culture study to see the presence of any micro-organism associated with inflammation.

Conclusion

From the present observation, it is felt that the presence of inflammation in cervical cytology smears should be taken with caution and an attempt should be made for the culture of vaginal swab of the women to know if any micro-organism is present. This will facilitate the adequate treatment of inflammation and would help the gynaecologist to manage the patient more properly. Further, such a procedure will also help in checking the persistence of inflammation which has been widely implicated in the development of precancerous changes in the cervix. The present investigators have also found a high percentage of LSIL in women with inflammatory smears. It appears that the inflammation had been pre-existing when the cervical cytological examination was conducted and SIL was detected. A high percentage of pre-existing inflammation in women in whom inflammatory smears were detected on cytology might be the reason for a high incidence of SIL. Hence all women showing inflammatory smears should be adequately treated and subjected to yearly cytological follow up to rule out any persistence of inflammation or subsequent development of premalignancy.

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