SSR Institute of International Journal of Life Sciences
ISSN (O): 2581-8740 | ISSN (P): 2581-8732
Chauhan *et al*., 2025
doi: 10.21276/SSR-IIJLS.2025.11.4.15

Original Article

open access

# Study Analysing Association of Inflammatory Biomarkers with Cervical Intraepithelial Neoplasia Lesions

**Shalini Singh Chauhan[1]*, Kavita N. Singh[2], Kirti Patel[3]**

[1]Post-graduate, Department of Obstetrics and Gynaecology, NSCB Medical College, Jabalpur (M.P.), India
[2]Dean, Gandhi Medical College, Bhopal (M.P.), India, Former Head of Department, Department of Obstetrics and Gynaecology, NSCB Medical College, Jabalpur (M.P.), India
[3]Assistant Professor, Department of Obstetrics and Gynaecology, NSCB Medical College, Jabalpur (M.P.), India

***Address for Correspondence:** Dr. Shalini Singh Chauhan, Postgraduate, Department of Obstetrics and Gynaecology, NSCB Medical College, Jabalpur (M.P.), India
**E-mail:** shalinichauhan209@gmail.com

**Received: 18 Feb 2025/ Revised: 15 Apr 2025/ Accepted: 18 Jun 2025**

## ABSTRACT

**Background:** Inflammation plays a key role in cancer development, including cervical cancer. The progression from CIN to cervical cancer involves viral, genetic, and immune factors. Inflammatory biomarkers like C-reactive protein (CRP) and lactate dehydrogenase (LDH) have gained attention for their potential association with CIN. These markers reflect the inflammatory and metabolic environment of cervical carcinogenesis. This study aimed to assess the association of serum CRP and LDH with cervical intraepithelial neoplasia.

**Methods:** All women attending the outpatient department of NSCB Medical College, Jabalpur, during the study period, with inclusion criteria, were screened by Pap smear and VIA. For every screen-positive case, estimation of serum CRP and serum LDH was done.

**Results:** Among 3368 women screened by Pap smear and VIA, 70 were screen positive. Serum CRP was <3 mg/L in 9.8%, 3–10 mg/L in 55.7%, and 10–100 mg/L in 34.4% of cases, showing a significant association with CIN (p=0.04). Serum LDH was 140–280 U/L in 6.6%, 281–500 U/L in 55.7%, and >500 U/L in 37.7%, also showing a significant association with CIN (p=0.03). Nine lost-to-follow-up cases were excluded.

**Conclusion:** Our results demonstrate that elevated serum CRP and LDH levels are significantly associated with higher grades of CIN. Serum CRP and LDH levels could be used as adjunctive markers to improve the accuracy of CIN diagnosis and to monitor disease progression. Incorporating these biomarkers into screening protocols may enhance early detection and allow for more tailored treatment approaches.

**Key-words:** Cervical intraepithelial neoplasia (CIN), Human Papilloma Virus (HPV), C-reactive protein (CRP), Lactate Dehydrogenase (LDH)

## INTRODUCTION

Cervical cancer is still a major worldwide and Indian public health concern. It ranks as the fourth most prevalent cancer among women worldwide. In 2018, approximately 570,000 women were diagnosed with cervical cancer, accounting for 6.6% of all cancers in women, and around 311,000 women died from the disease [1]. Cervical cancer has a prolonged precancerous stage, known as Cervical Intraepithelial Neoplasia (CIN), which can be detected early through screening methods such as Pap smear, visual inspection with acetic acid or Lugol's iodine, and HPV DNA testing [2]. This early detection has significantly improved treatment outcomes. Inflammation is increasingly recognized as a contributor to cancer development, including cervical cancer [3-5]. A low-grade inflammatory status gene signature, which lies between tissue homeostasis and classic inflammation, has been found in a variety of tumors by recent research [6], indicating that

**How to cite this article**
Chauhan SS, Singh KN, Patel K. Study Analysing Association of Inflammatory Biomarkers with Cervical Intraepithelial Neoplasia Lesions. SSR Inst Int J Life Sci., 2025; 11(4): 7900-7906.

**Access this article online**
https://iijls.com/

 

doi: 10.21276/SSR-IIJLS.2025.11.4.15

inflammation contributes to the development of cancer [7].

In cervical cancer, limited studies have examined the relationship between systemic [8–10] or cervical (local) inflammation [11–14] and the risk of persistent HPV infection and cervical precursor progression, generally finding a positive correlation [8–14]. CRP, a systemic inflammatory biomarker produced by the liver during inflammation, is widely used in clinical practice. Recent studies indicate that CRP is positively associated with various cancers [15–18]. However, the impact of CRP on cervical lesions remains underexplored. The progression of CIN to cervical cancer involves a complex interplay of viral, genetic, and immunological factors. Among these, the role of inflammatory biomarkers has gained considerable attention. CRP and LDH are two such biomarkers that have been investigated for their potential association with CIN.

The liver produces the acute-phase protein known as CRP in response to inflammation. It is a well-established marker of systemic inflammation and has been linked to various malignancies. Elevated CRP levels are indicative of an ongoing inflammatory process, which may contribute to the development and progression of neoplastic changes. In the context of CIN, inflammation driven by human papillomavirus (HPV) infection, a major etiological factor for CIN, can lead to increased CRP levels. Studies have suggested that higher CRP levels might correlate with the severity of CIN, reflecting the degree of underlying inflammation.

Pyruvate is converted to lactate anaerobically by the enzyme LDH. It is released into the bloodstream during tissue damage and cell turnover, making it a marker of cellular injury and metabolic stress. Elevated LDH levels have been observed in various cancers, including cervical cancer, and are often associated with poor prognosis. In the context of CIN, increased LDH levels may indicate heightened cellular turnover and metabolic activity within the dysplastic epithelium. This association highlights the potential of LDH as a biomarker for identifying high-risk CIN lesions [4].

The potential link between CRP, LDH, and CIN underscores the significance of the inflammatory and metabolic microenvironment in cervical carcinogenesis. By understanding the roles of these biomarkers, researchers and clinicians can better stratify patients based on risk, monitor disease progression, and potentially develop targeted interventions to mitigate the progression of CIN to invasive cervical cancer. Furthermore, the measurement of CRP and LDH levels could complement existing screening and diagnostic tools, providing a more comprehensive assessment of patient status [3,5].

## MATERIALS AND METHODS

**Study Design**- It was a prospective observational study carried out in the department of Obstetrics and Gynaecology at Netaji Subhash Chandra Bose Medical College, Jabalpur, from June 2022 to July 2024.

### Sample Size

- All women attending the outpatient department of Obstetrics and Gynaecology, who were screened positive for pre-invasive cervical lesions in the duration of study.

### Inclusion Criteria

- Screen positive cases (HPV, Cytology and VIA)
- Histologically proven CIN I, II and III

### Exclusion criteria

- Unmarried females
- Pregnant females
- With complaint of bleeding per vaginum at the time of examination
- Proved cases of carcinoma cervix or frank growth on the cervix
- Women with other inflammatory conditions, recent infections or treatments that might affect CRP and LDH levels.

**Methodology-** All women attending the outpatient department of NSCB Medical College, Jabalpur, during the study period, with the inclusion criteria, were screened by Pap smear and VIA.

All VIA-positive women were subjected to colposcopy and false-positive cases were returned for routine screening after the lesion was assessed using the RCI score. Colposcopy-guided biopsy was taken in cases with RCI score more than 2. Further treatment was instituted based on the biopsy report. Cases with RCI score 0 to 2, who were willing and eligible for screening and treat in the same visit, were subjected to thermal ablation or given conservative management and put on follow-up.

 

doi: 10.21276/SSR-IIJLS.2025.11.4.15

Biopsy was not required in cases with RCI score 0-2 as they are colposcopically low-grade lesions.

Five millilitres of venous blood were extracted from each participant's antecubital vein while taking all necessary aseptic precautions for each screen-positive instance. Centrifugation was used to separate the serum after the blood had been allowed to clot. Serum LDH and CRP levels were estimated.

**Statistical Analysis-** Data were analyzed using SPSS version 26. Categorical variables were expressed as percentages. The association between CRP, LDH levels, and CIN grades was assessed using Fisher's Exact Test. A p-value <0.05 was considered statistically significant.

**Ethical Clearance**- The present study has been approved by the Institutional Ethics Committee, N.S.C.B Medical College, Jabalpur, M.P. Written consents were taken from women after explaining the advantages and steps of examination and treatment by thermoablation and follow-up.

## RESULTS

Table 1 summarizes the demographic characteristics of the 70 screen-positive women. It includes age distribution, parity, locality (rural/urban), and occupation. The majority of women were between 26–35 years of age, most were multiparous (para 2 or 3), and an equal distribution was seen between rural and urban populations. Most participants were housewives.

**Table 1:** Demographic profile

| Demographic features | No. of cases (n=70) | Percentage |
|---|---|---|
| Age (in years) | | |
| 26-30 | 24 | 34.3% |
| 31-35 | 20 | 28.6% |
| 36-40 | 08 | 11.4% |
| >40 | 18 | 25.7% |
| Parity | | |
| 0 | 08 | 11.4% |
| 1 | 07 | 10% |
| 2 | 31 | 44.3% |
| 3 | 16 | 22.9% |
| 4 | 05 | 7.1% |
| 5 | 03 | 4.3% |
| Locality | | |
| Rural | 35 | 50% |
| Urban | 35 | 50% |
| Occupation | | |
| Daily wage worker | 02 | 2.9% |
| Farmer | 05 | 7.1% |
| Housewife | 61 | 87.1% |
| Service | 01 | 1.4% |
| Others | 01 | 1.4% |

Table 2 presents the histopathological outcomes of the 70 screen-positive cases. It shows the number and percentage of women diagnosed with cervicitis, CIN I, CIN II, and CIN III based on biopsy. It also includes those lost to follow-up and those who did not require biopsy (RCI score 0–2). CIN I was the most common lesion observed (34.3%).

**Table 2:** Distribution of cases according to cervical biopsy report

| Cervical biopsy report | No. of cases | Percentage |
|---|---|---|
| Cervicitis (biopsy proven) | 09 | 12.9% |
| CINI (biopsy proven) | 24 | 34.3% |
| CIN II (biopsy proven) | 08 | 11.4% |
| CIN III (biopsy proven) | 03 | 4.3% |
| Lost to follow up | 09 | 12.9% |
| RCI score 0-2 (Biopsy not required) | 17 | 24.3% |
| Total | 70 | 100% |

Table 3 illustrates the relationship between CRP levels and biopsy-proven cervical lesions. It categorises CRP values into three groups: <3 mg/L (normal), 3–10 mg/L (moderately elevated), and 10–100 mg/L (highly elevated). The table shows a progressive increase in CRP levels with the severity of CIN, with 100% of CIN III cases showing highly elevated CRP. This association was statistically significant (p=0.04).

Fig. 1 graphically represents the data from Table 3, demonstrating a trend of rising CRP levels with increasing CIN grade. It highlights the potential use of CRP as a marker for inflammation and severity in CIN cases.

 

doi: 10.21276/SSR-IIJLS.2025.11.4.15

**Table 3:** Association of cervical biopsy report with serum CRP levels

| CIN Grade | <3 mg/L | 3-10 mg/L | 10-100 mg/L | Total |
|---|---|---|---|---|
| Cervicitis (biopsyproven) | 0 (0%) | 7 (77.8%) | 02 (22.2%) | 09 |
| CIN 1 (biopsy proven) | 1 (4.2%) | 15(62.5%) | 08 (33.3%) | 24 |
| CIN II (biopsy proven) | 2 (25%) | 02 (25%) | 04 (50%) | 08 |
| CINIII (biopsy proven) | 0 (0%) | 00 (0%) | 03 (100%) | 03 |
| RCI score 0-2 (Biopsy not required) | 3 (17.6%) | 10 (58.8%) | 04 (23.5%) | 17 |
| Total | 6 (9.8%) | 34 (55.7%) | 21(34.4%) | 61 (100%) |

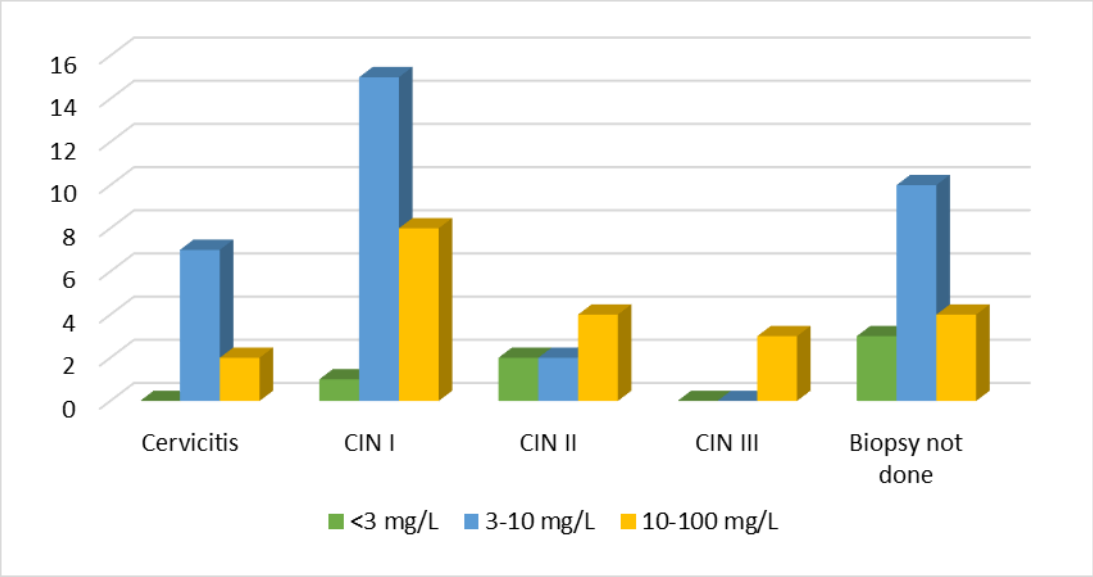


**Fig. 1:** Association of cervical biopsy report with serum CRP levels

Table 4 shows the distribution of serum LDH levels across biopsy-confirmed cases of cervicitis and CIN. LDH is categorized as normal (140–280 U/L), moderately elevated (281–500 U/L), and highly elevated (>500 U/L). A strong correlation is seen between higher CIN grades and elevated LDH levels. CIN III had 66.7% of cases with LDH >500 U/L. The association was statistically significant (p=0.03).

**Table 4:** Association of cervical biopsy report with serum LDH levels

| CIN Grade | 140-280 U/L | 281-500 U/L | >500 U/L | Total |
|---|---|---|---|---|
| Cervicitis (biopsy proven) | 00(0%) | 09(100%) | 00 (0%) | 09 |
| CIN 1(biopsy proven) | 01(4.2%) | 11(45.8%) | 12 (50%) | 24 |
| CIN II (biopsy proven) | 00(0%) | 03 (37.5%) | 05 (62.5%) | 08 |
| CIN III (biopsy proven) | 00(0%) | 01 (33.3%) | 02 (66.7%) | 03 |
| RCI score 0-2 (Biopsy not required) | 03(17.6%) | 10 (58.8%) | 04 (23.5%) | 17 |
| Total | 04 (6.6%) | 34(55.7%) | 23(37.7%) | 61(100%) |

 

doi: 10.21276/SSR-IIJLS.2025.11.4.15

Fig. 2 visualizes the trend from Table 4, showing that LDH levels increase with the severity of CIN. It supports the hypothesis that LDH is a potential metabolic biomarker for identifying high-risk cervical lesions.

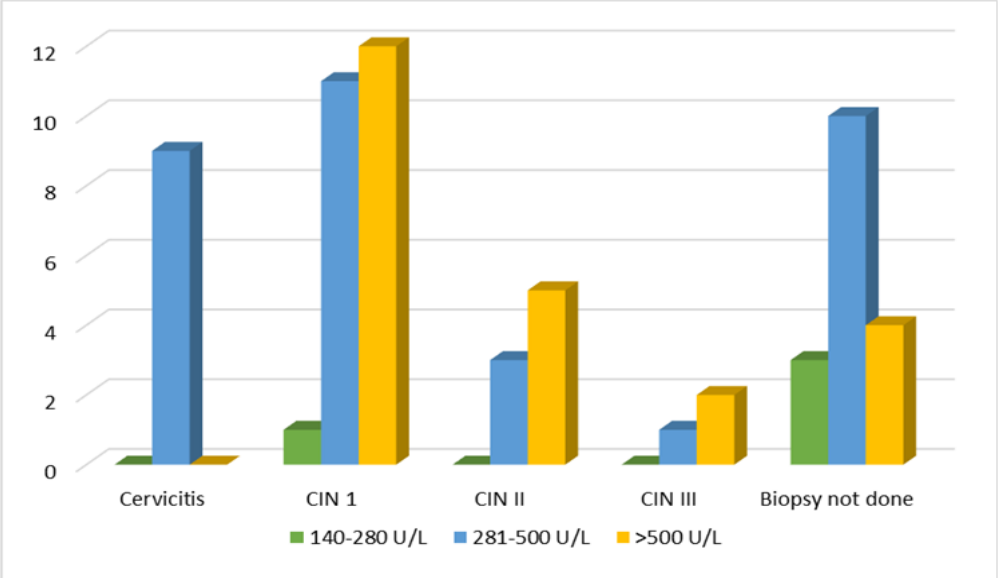


**Fig. 2:** Association of cervical biopsy report with serum LDH levels

## DISCUSSION

In the present study, 34.3% women were from age group 26–30 years, 28.6% women were from 31–35 years, and 11.4% women were from 36–40 years, so in total, majority of women, i.e. 74.3%, were from the age group 26–40 years. The mean age of cases in our study was 35.2 years, indicating that CIN is more prone to sexually active women. This goes in concordance with the study conducted by Bhattachan *et al.* [15], where the mean age group of the study population with a clinically unhealthy cervix was 38.17 years. Another study conducted by Goyal *et al.* [16], that the mean age of women subjected to VIA screening was 39.38 years. Previous studies agree well with this study that CIN is more prone to sexually active women.

Most women (44.3%) were para 2, and 22.9% were para 3; only 11.4% were nulliparous, indicating multiparity as a related risk for CIN. Amongst the presenting complaints, the most common presenting complaint was white discharge per vaginum, seen in 74.2% patients, followed by pain in the lower abdomen and menstrual complaints in 47.1% and 27.1% cases, respectively. Among other complaints, post coital bleeding was seen in 5.7%, itching in 12.8%, and burning micturition reported in 17.1% cases.

In our study, 84.3% women had type 1 TZ and 15.7% women had type 2 TZ. Type 3 TZ was excluded from our study.

This shows that the women treated had a visible transformation zone, as the eligibility criteria. Begum *et al.* [17], according to their study, during the past 50 years, the incidence and death of cervical cancer have been lowered by up to 80% in developed nations, thanks to population-based cervical cytology screening programs that use Pap smear testing every three to four years. According to a population-based study by Nayir *et al.* [18], cervical cancer is on the decline in developing nations like India.

In this study, women were screened by cytology and VIA, and those who tested positive were included. Women with RCI score >2 were subjected to colposcopy-guided biopsy. They came later with biopsy reports, with CIN I reported in 34.3%, CIN II in 11.4%, CIN III in 4.3% and cervicitis in 12.9%. 9 women (12.9%) did not follow up with the biopsy report. Biopsy was not done in 24.3% women who had RCI score 0–2 and were given conservative management and put on follow-up. In the study conducted by Sreedevi *et al.* [19], 20.6% cases had cervicitis, 46.39% had CIN I, 12.37% had CIN II, and 4.12% had CIN III. A study by Taslima Kasem *et al.* [20] showed cervicitis in 40%, and CIN I, II, and III were reported in 20%, 15%, and 10% respectively.

In our study, the normal range of serum CRP level <3 mg/L found in 9.8% screen-positive cases, moderately elevated serum CRP levels (3–10 mg/L) seen in 55.7% cases, and highly elevated levels (10–100 mg/L) seen in

 

doi: 10.21276/SSR-IIJLS.2025.11.4.15

34.4% cases. There were nine cases of loss to follow up, which are not included in the above statistics. An increase in serum CRP levels with increasing severity of CIN has been observed in this study. 33.3% cases with CIN I, 50% cases with CIN II and 100% cases with CIN III had serum CRP levels in the range 10–100 mg/L.

A p-value of 0.04 indicates that the association of raised serum CRP levels with CIN lesions is statistically significant. Normal range of serum LDH levels (140–280 U/L) found in 6.6% cases, moderately elevated levels (281–500 U/L) found in 55.7% cases and highly elevated levels (>500 U/L) in 37.7% cases. There were nine cases of loss to follow up, which are not included in the above statistics.

A p-value of 0.03 indicates a statistically significant association between raised serum LDH levels and CIN lesions. 50% cases with CIN I, 62.5% cases with CIN II and 66.7% cases with CIN III had LDH levels >500 U/L. With the increasing severity of CIN, the proportion of cases with markedly elevated LDH levels (>500 U/L) has also increased. The mean LDH level in CIN cases in our study was 482.88 U/L. This correlates well with the study conducted by Akter *et al.* [21], where the mean LDH levels in cases with cervical cancer were 487.8 U/L.

## CONCLUSIONS

We have concluded that the elevated serum CRP levels are significantly associated with higher grades of CIN. This suggests that CRP, a marker of inflammation, may play a role in the pathogenesis of cervical lesions. Chronic inflammation is known to contribute to the development of various cancers, and our findings support the hypothesis that inflammatory processes are involved in the progression of CIN. Similarly, elevated serum LDH levels were found to correlate with higher grades of CIN. LDH is an enzyme involved in glycolysis, and its increased levels are often associated with cellular damage and metabolic changes in neoplastic cells. The association of high LDH levels with advanced CIN grades underscores the potential of LDH as a marker for cellular dysregulation in cervical neoplasia. These findings have important clinical implications. Serum CRP and LDH levels could be used as adjunctive markers to improve the accuracy of CIN diagnosis and to monitor disease progression. Incorporating these biomarkers into screening protocols may enhance early detection and allow for more tailored treatment approaches.

## CONTRIBUTION OF AUTHORS

**Research concept-** Shalini Singh Chauhan, Kavita N. Singh
**Research design-** Shalini Singh Chauhan, Kavita N. Singh
**Supervision-** Kavita N. Singh, Kirti Patel
**Materials-** Shalini Singh Chauhan, Kirti Patel
**Data collection-** Shalini Singh Chauhan
**Data analysis and interpretation-** Shalini Singh Chauhan, Kirti Patel, Kavita N. Singh
**Literature search-** Shalini Singh Chauhan
**Writing article-** Shalini Singh Chauhan, Kirti Patel, Kavita N. Singh
**Critical review-** Kavita N. Singh
**Article editing-** Shalini Singh Chauhan, Kirti Patel
**Final approval-** Kavita N. Singh

## REFERENCES

[1] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin., 2018; 68(6): 394–424.
[2] American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 463: Cervical cancer in adolescents: screening, evaluation, and management. Obstet Gynecol., 2010; 116(2 Pt 1): 469–72.
[3] Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. Nature. 2008; 454: 436–44.
[4] Boccardo E, Lepique AP, Villa LL. The role of inflammation in HPV carcinogenesis. Carcinogenesis, 2010; 31: 1905–12.
[5] Parida S, Mandal M. Inflammation induced by human papillomavirus in cervical cancer and its implication in prevention. Eur J Cancer Prev., 2014; 23: 432–48.
[6] Medzhitov R. Origin and physiological roles of inflammation. Nature, 2008; 454: 428–35.
[7] Aran D, Lasry A, Zinger A, et al. Widespread parainflammation in human cancer. Genome Biol., 2016; 17: 145–45.
[8] Kemp TJ, Hildesheim A, García-Piñeres A, et al. Elevated systemic levels of inflammatory cytokines in older women with persistent cervical human papillomavirus infection. Cancer Epidemiol Biomarkers Prev., 2010; 19(8): 1954–59.
[9] Sharma A, Rajappa M, Saxena A, Sharma M. Cytokine profile in Indian women with cervical intraepithelial neoplasia and cancer cervix. Int J Gynecol Cancer, 2007; 17: 879–85.

 

doi: 10.21276/SSR-IIJLS.2025.11.4.15

[10]Kadish AS, Timmins P, Wang Y, et al. Regression of cervical intraepithelial neoplasia and loss of human papillomavirus (HPV) infection is associated with cell-mediated immune responses to an HPV type 16 E7 peptide. Cancer Epidemiol Biomarkers Prev., 2002; 11: 483–88.

[11]Hammes LS, Tekmal RR, Naud P, et al. Macrophages, inflammation and risk of cervical intraepithelial neoplasia (CIN) progression—clinico-pathological correlation. Gynecol Oncol., 2007; 105: 157–65.

[12]Castle PE, Hillier SL, Rabe LK, et al. An association of cervical inflammation with high-grade cervical neoplasia in women infected with oncogenic human papillomavirus (HPV). Cancer Epidemiol Biomarkers Prev., 2001; 10: 1021–27.

[13]Davidson B, Goldberg I, Kopolovic J. Inflammatory response in cervical intraepithelial neoplasia and squamous cell carcinoma of the uterine cervix. Pathol Res Pract., 1997; 193: 491–95.

[14]Tjiong MY, van der Vange N, ten Kate FJ, et al. Increased IL-6 and IL-8 levels in cervicovaginal secretions of patients with cervical cancer. Gynecol Oncol., 1999; 73: 285–91.

[15]Bhattachan K, Dangal G, Karki A, Pradhan H, Shrestha R, et al. Evaluation of abnormal cervix with visual inspection under acetic acid and colposcopy. J Nepal Health Res Counc., 2019; 17: 76–79.

[16]Goyal S, Tandon P, Bhutani N, Gill B. To study the role of visual inspection of cervix with acetic acid (VIA) in cervical cancer screening. Int J Reprod Contracept Obstet Gynecol., 2014; 3: 684–87.

[17]Begum F, Kasem SB, Razzaque SA, Adiba R, Anika S. Role of colposcopy in the evaluation of visual inspection of cervix with acetic acid-positive cases of unhealthy cervix. J South Asian Feder Menopause Soc., 2017; 5(2): 102–06.

[18]Nayir T, Okyay RA, Nazlican E, Yesilyurt H, Akbaba M, et al. Cervical cancer screening in an early diagnosis and screening center in Mersin, Turkey. Asian Pac J Cancer Prev., 2015; 16(16): 6909–12.

[19]Sreedevi A, Javed R, Dinesh A. Epidemiology of cervical cancer with special focus on India. Int J Womens Health, 2015; 7: 405–14.

[20]Kasem SB, Razzaque SA, Adiba R, Anika S, Banik M. Colposcopic evaluation of visual inspection with acetic acid positive cases of unhealthy cervix. J Bangladesh Coll Physc Surg., 2019; 37(2): 60–65. doi: 10.3329/jbcps.v37i2.40561.

[21]Akter T, Siddika A, Akter K, Akhter S, Haque MA, et al. Colposcopic findings of cervix in VIA (Visual Inspection of Cervix by Acetic Acid) positive cases at BSMMU, Dhaka, Bangladesh. Sch Int J Obstet Gynec., 2022; 5: 9.