

SERUM INTERLEUKIN-10 LEVELS IN PATIENTS WITH CERVICAL NEOPLASIA: A CROSS-SECTIONAL STUDY FROM EASTERN INDIA

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ABSTRACT

Background: Cervical cancer is the most common gynaecological malignancy in India women. Limited studies have reported the association of multifunctional cytokine interleukin-10 (IL-10) in different malignancies including cervical cancer. In this study we examined the serum IL-10 levels in patients with cervical cancer in eastern region of India. This study was carried out in a tertiary care hospital located in eastern region of India. Serum samples were collected from the subjects with cervical neoplasia and compared with healthy controls. The levels of IL-10 were measured by enzyme-linked immunosorbent assay (ELISA) in both groups and compared for the clinical correlation. Statistical analysis employed SPSS 13.0, applying various non-parametric and parametric tests to assess differences, with a significance threshold set at $p < 0.05$. This study included 64 confirmed cervical cancer cases and 28 healthy controls. The mean age of cervical cancer patients was 54.03 ± 8.36 years. The serum IL-10 levels were elevated in subjects with cervical neoplasia compared to the healthy controls ($p=0.0001$). This research demonstrates that the IL-10 levels significantly elevated than those in control group, suggesting its potential as a biomarker and its involvement in cervical neoplasia. Additional studies with a larger sample size needed to ascertain the findings

KEYWORDS: Cervical neoplasia, cytokine, IL-10, CIN, ELISA, India

INTRODUCTION

Cervical cancer ranks as the fifth most frequently diagnosed cancer among women worldwide with an estimated of 661,021 new cases and around 348,189 deaths annually in 2024³. Cervical cancer incidence and mortality rates are highest in low- and middle-income countries. It is the most common cancer seen in Indian women². Human papillomavirus (HPV) infection is the predominant risk factor for cervical cancer in women. While persistent infection with high-risk HPV strains is recognized as the primary cause of cervical malignancies, it is insufficient and other factors may be involved to trigger the tumorigenesis^{13,16,19}. This underscores the secondary and environmental factors in the progression of cervical cancer. Moreover, it is confirmed from the fact that majority of HPV infection are transient and cleared harmlessly by host immune system.

This confirmed the fact that HPV exposure alone is insufficient to drive full scale oncogenesis without the interventions of secondary co-factors²². Besides HPV infection other risk factor associated with cervical cancer includes early marriage age, tobacco use, low socioeconomic status and parity^{7,10,24}. In a majority of cases women infected with HPV, approximately 90% of cases infections are resolved by the immune system¹¹. However, the detail mechanisms underlying this immune clearance remains unclear. Host immune response is crucial in the development of cervical neoplasia⁹. HPV infection influences systemic immune response which is reflected by circulating inflammatory cytokine levels²¹.

In cervical malignancy there is a pathological shift occurs from cell-mediated Type 1 immune response towards immunosuppressive Type 2 response¹⁴. During cervical cancer development serum levels of pro-inflammatory cytokines such as TNF- α , IL 6, IL-1 β are frequently elevated to promotes tissue remodelling and tumour cell survival¹⁷, alternatively, alterations in levels of anti-inflammatory cytokines like IL 10 suppresses anti-tumour immunity by impairing antigen specific T-cell proliferation¹⁷. Evaluation of these inflammatory cytokines in the serum of patients with cervical cancer will helps us to understand host immune landscape. Further, understanding how tobacco smoking interacts and impact levels of inflammatory cytokines during cervical cancer progression is crucial. This will be helpful in deducing potential biomarkers and therapeutic targets associated with the progression of cervical cancer. This study aims to examine the cytokine IL 10 levels in serum in patients with cervical neoplasia.

MATERIALS & METHODS:

Study population: This cross-sectional study was carried out at the Department of Obstetrics and Gynaecology, and Cancer Hospital, Kalinga Institute of Medical Sciences, a tertiary care hospital in eastern India. The subjects enrolled were included between July 2023 through March 2024. Institutional Ethics Committee approval obtained for the study protocol from Kalinga Institute of Medical Sciences, KIIT University, Bhubaneswar (Ref. No. KIIT/KIMS/IEC/1346/2023). Women diagnosed with cervical neoplasia through PAP smear, low-grade disease, and high-grade disease based on histological diagnosis were included in the study. Women with prior conditions with malignancy, under immunosuppressive treatment, pregnancy, less than 18 years of age were excluded from study. The study also incorporated age matched healthy controls, and data regarding socio-demographic and lifestyle factors were collected using a pre-established questionnaire.

Study Sampling: Four ml of venous blood samples were collected in red top blood collection tube and transported to the laboratory. Serum separated from blood samples and processed immediately or stored at -80°C until used by enzyme linked immunosorbent assay (ELISA).

Estimation of serum cytokines: The serum concentrations of cytokine interleukin 10 (IL-10) was measured using commercial ELISA kit (FINETEST, Wuhan Fine Biotech Co Ltd, China, catalogue number: EH-0173) as per manufacturer's instructions. In brief, 100 μL of serum samples added into respective of the ELISA plate well, pre coated with anti IL-10 antibody and incubated for 90 minutes at 37°C . Following this incubation, the plate was washed twice without immersion. Subsequently, 100 μL of a working solution containing biotin-labelled antibody was added to each well, the plate was sealed, and incubation continued for 60 minutes at 37°C . After washing the plate three times, 100 μL of HRP-Streptavidin Conjugate working solution was added to each well, followed by sealing the plate and static incubation for 30 minutes at 37°C . The plate was then washed five times, with each wash lasting one minute. Next, 90 μL of TMB substrate solution was added, and incubation occurred for 20 minutes at 37°C . Finally, 50 μL of stop solution was added, and the plate was read at 450 nm using a microplate reader (MultiSkan Sky, Thermo Scientific, USA). The concentration of IL-10 in the samples was determined by constructing a standard curve, with the concentration of the target substance being proportional to the OD 450 value.

Statistical analysis: SPSS 13.0 software program (SPSS, Chicago, IL, USA) used for Statistical analysis. The analysis of non-parametric variables involved the application of the Mann-Whitney U test, Kruskal-Wallis test, and subsequent Post-Hoc Pairwise Tests were utilized. Fisher's exact test used for categorical variables. A p-value of less than 0.05 was deemed statistically significant.

RESULTS:

During the study period, serum samples collected from a total of 64 women diagnosed with cervical neoplasia and 28 age matched healthy controls were included in the study. Patients with cervical neoplasia cases have a mean age of 54.03 ± 8.36 years and mostly from the age range from 21 to 81 years. Majority of study population presented from rural population (71.88%). Among the population examined 54.68% reported to have smoking habit. Majority of them had 1-2 pregnancies (82.81%). While 17.18% reported to have more than >3 pregnancies [Table 1]. Among the cervical neoplasia group, of 64 cases examined, histologically proven invasive cancer seen in 12 (18.75%) cases. When compared for the serum IL-10 levels, the patients with cervical neoplasia have higher levels in compared to healthy controls. Further, while measuring the serum concentration of anti-inflammatory cytokine IL 10 between in healthy controls, patients with neoplasia have significantly elevated levels IL=10 expression ($p = 0.0001$) [Figure 1].

Table 1: Baseline clinic-demographic characteristics of the study participants (n=64)

Characteristics	Frequency (%)
<i>Age (years)</i>	
Range	21- 81
< 30	12 (18.75%)
31-50	14 (21.87%)
51-60	23 (35.93%)
61-70	11 (17.18%)
> 70	04 (6.25%)
Mean	54.03 ± 8.36
<i>Population distribution</i>	
Rural	46 (71.88%)
Urban	18 (28.12%)
<i>Smoking status</i>	
Non-smoking	35 (54.68%)

Smoking	29 (45.31%)
<i>Marital status</i>	
Married	58 (90.62%)
Unmarried	06 (9.37%)
<i>No. of pregnancies</i>	
1-2	53 (82.81%)
> 3	11 (17.18%)

Age in years, data were represented in mean $\pm$ SD, numbers and percentage

Figure 1: Serum IL-10 concentration (pg/mL) among healthy controls and patients with cervical neoplasia

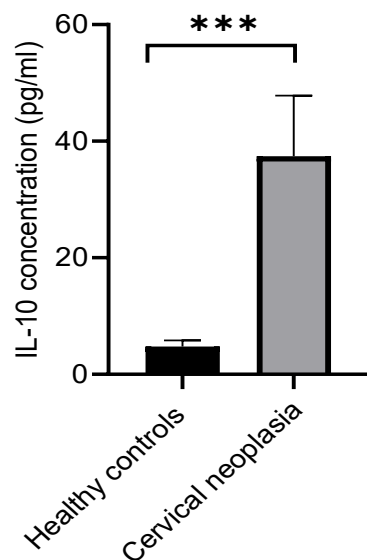


Figure shows the mean concentration of IL-10 among cervical neoplasia cases (n=64) and healthy controls (n=28). Mann–Whitney U test was performed to test the significance among the groups. [A p value of < 0.05 was deemed statistically significant (* = $p < 0.05$, ** = $p < 0.01$ and *** = $p < 0.001$)].

DISCUSSION

The host immune microenvironment plays a critical role in the pathogenesis and progression of cervical cancer. While high-risk human papillomavirus HPV infection is recognized as the primary etiological driver, where as host immune response and the resulting systemic inflammatory alterations are pivotal in determining whether an infection clears or progresses to invasive malignancy. This study evaluated the sociodemographic profiles, smoking status, and serum levels of key cytokine IL-10 cytokines among cervical cancer patients and healthy controls. The mean age in patients with cervical neoplasia in this study was found to be 54.03 ± 8.36 years. This age display is consistent with the established natural history of cervical carcinogenesis, which typically involves a prolonged latency period of 15 to 20 years following persistent high-risk HPV exposure. Cervical screening for women aged 50 to 64 years significantly influences cervical cancer incidence during this age group and also for many subsequent years⁵.

Interleukin (IL-10) is a multifunctional cytokine plays a crucial role in regulating inflammation and modulating immune response^{1,4,15}. In the case of HPV-associated malignancies, viral oncoproteins E6 and E7 are known to upregulate IL-10 expression to forge a local and systemic immunosuppressive microenvironment²⁰. The levels of anti-inflammatory cytokine IL-10 demonstrated clear statistical significance in our study. Our findings of increased serum IL-10 levels in patients with cervical neoplasia align consistent with the recent clinical trial conducted in 2025¹², which found that systemic immune down-regulation and elevated levels of immunosuppressive cytokines, such as IL-10, TGF-beta correlate directly with high-grade cervical neoplasia and tumor growth. Additionally, a large-scale clinical validation study in 2024⁶ confirmed that serum IL-6 and IL-10 levels rise concurrently during the progression of malignancy, indicating their dual markers of immune evasion and poor long-term outcomes.

The elevation of serum IL-10 is known to inhibit anti-tumor activity by downregulating major histocompatibility complex (MHC) molecules and impairing the proliferation of antigen specific T cells^{8,18}. This study has a limitation in the cross-sectional and limited sample size. Future prospective studies with larger, multi-centric cohorts are required to validate these trends.

The immune profile of these patients reveals a clear transition towards immunosuppressive condition, evidenced

by notable increase in the anti-inflammatory IL-10 cytokine within the subjects with cervical neoplasia when compared to healthy individuals. This is in consistent with the finding of elevated IL-10 in high grade lesion and in malignancy of the cervix¹⁴. This significant rise in IL-10 may foster a protective microenvironment that hinders anti-tumor T cell activity²³. This study underscores the intricate interplay between host immunoregulation, role of IL-10 in promoting an immunosuppressive environment in the cervix, thereby aiding progression of cervical cancer.

CONCLUSION

The serum levels of IL-10 were elevated in subjects with cervical neoplasia compared to the healthy controls. Elevated cytokine levels may play a role in promoting inflammation in tumorigenesis. Additional studies with a larger sample size needed to ascertain the findings.

Conflicts of Interest: There is no potential conflicts of interest

Author Contributions: SKP, SJ, SRN experiments and analysis of the data, JP, AD, BKB, RG, DP, ARKP study design and mentoring, SKP, SRN and ARKP wrote the manuscript. All authors have seen and approved the manuscript.

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Ethical Clearance Information: This study was approved from Institute Ethics Committee, approval number (Ref No. KIIT/KIMS/IEC/1346/2023).

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