Research Article

Interleukin-6 levels in the serum of patients with cervical neoplasia at a tertiary care centre in Odisha, India

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Abstract

Cervical cancer represents the most prevalent gynaecological malignancy among Indian women. Conflicting evidence has been observed regarding the production of Il-6 levels in cervical neoplasia. This study aimed to evaluate serum interleukin-6 (IL-6) concentrations and examined their correlation with disease severity among patients diagnosed with cervical neoplasia in eastern India. Serum samples were obtained from individuals diagnosed with cervical neoplasia and were compared to those from healthy controls. Estimation of the levels of Il-6 in both groups were quantified using enzyme-linked immunosorbent assay (ELISA) to assess clinical correlations. Statistical analysis was conducted using GraphPad Prism software, and a p-value of less than 0.05 was deemed statistically significant.This study included 71 cervical neoplasiacases.Majority subjects presented in 41-50 years age group (23.84%). Serum IL-6 levels were significantly higher in individuals with cervical neoplasia when compared to healthy controls (p=0.001). Levels of IL-6 found in the patients were markedly elevated compared to serum levels in the controls. Overall, the observation that elevated IL-6 levels indicates a possible down-regulation of tumour-specific immune responses in cervical neoplasia, contributing to promote tumour progression.Further investigation involving a larger sample size is essential to obtain a more accurate representation of the findings.

Keywords: Interleukin-6, CIN, Cervical lesions, ELISA, India

1. Introduction

Globally, cervical cancer represents a critical public health challenge and ranks among the leading causes of cancer-related mortality in women. In India, it constitutes the most frequently diagnosed gynaecological malignancy [Bhatla et al., 2008], contributing substantially to the overall disease burden with an estimated 127,526 incident cases and 79,906 related deaths recorded annually [Bray et al., 2022; Jena et al., 2026]. Human papillomavirus (HPV) infection is a major risk factor for cervical cancer. While persistent infection with high-risk human papillomavirus (hr-HPV) is recognized as an obligate etiological agent in cervical carcinogenesis, it is insufficient to drive malignant transformation independently; rather, neoplastic progression is modulated by secondary host and environmental cofactors. This finding confirmed that HPV exposure alone is insufficient to cause full-scale oncogenesis without the involvement of secondary cofactors [Burd EM 2003, Wang et al, 2009, Blanco Ret al.,2024].

Most HPV infections are transient and are cleared from the cervical mucosa by the host immune system. This immune response is considered essential for viral clearance, while immunocompromised individuals, including women living with HIV, are more susceptible to HPV-related cervical lesions [Tisler et al., 2024,Wongkalasin N et al., 2025, Meglic E, et al., 2026]. However, the mechanisms underlying immune-mediated HPV clearance remain incompletely understood [Vallejo-Ruiz V, et al., 2024, Xia et al., 2025].

The host immune response is central to the development of cervical neoplasia [Hibma MH et al., 2012, Kiamba EW et al, 2025]. HPV infection can alter systemic immunity, as reflected in circulating cytokine levels [Paradkar et al., 2014, Vitkauskaite A et al., 2020]. Interleukin-6 (IL-6), a multifunctional pro-inflammatory cytokine, regulates immune responses and acute-phase reactions and helps defend against infection and tissue injury. IL-6 levels may rise substantially during persistent high-risk HPV infection and associated cervical lesions, where the cytokine may contribute to immune defence against HPV-related neoplasia. Selected studies indicate that cytokines such as IL-1β,

TNF-α, IL-10, and IL-6 are frequently elevated and may contribute to cervical cancer development [Saha et al., 2025, Cao et al., 2026, Padhi S et al., 2026].

IL-6 may also enhance cancer-cell survival and angiogenesis, with higher levels associated with persistent high-risk HPV infection, advanced disease, and poorer outcomes [Obeagu et al., 2025]. These findings highlight potential biomarkers and therapeutic targets for monitoring and addressing cervical cancer progression.Research on the relationship between IL-6 and cervical neoplasia remains limited, particularly regarding serum IL-6 levels in this specific region. This study seeks to quantify serum IL-6 expression and assess its prognostic implications for patients diagnosed with cervical neoplasia.

2. Materials & methods

Study population: Study design: cross-sectional. Patients presenting with various cervical lesions to the Obstetrics and Gynaecology department of Kalinga Institute of Medical Sciences, a tertiary care facility located Odisha, India, (during November 2023 to June 2024) were included in the study. Each study participant underwent clinical examination and supplemented by pertinent laboratory tests.

This study was approved from the institute ethics committee for human subjects and samples obtained after the study participants provided informed written consent. The study also included age-matched healthy controls, and information on socio-demographic information collected. Women with prior conditions with malignancy, under immunosuppressive treatment, pregnancy, less than 18 years of age and those participant does not consented for participation, were excluded from study.

Study Sampling

Venous blood samples of four milliliters were collected in serum collection tubes (contain no anticoagulant or contain a clot activator)and subsequently transported to the laboratory. The serum was separated from the blood samples and either processed immediately or stored at −80 °C for later use in ELISA.

Estimation of serum cytokines

The serum levels of interleukin 6 (IL-6) was quantified using a commercial ELISA kit [FINETEST IL-6 kit, cat no EH0201following the manufacturer's protocol.In the IL-6 ELISA procedure, 100 µL of serum samples were added to the appropriate wells of an ELISA plate that had been pre-coated with anti-IL-6 antibodies. This step followed by a 90-minute incubation period at 37°C, after which the plates were washed twice without immersion.

Subsequently, a working solution containing biotin-labelled antibodies specific to each target was added to the wells, and the plates were sealed for an additional 60-minute incubation at 37°C. Following three washes of the plate, 100 µL of the Streptavidin Horseradish Peroxidase (Streptavidin -HRP), Conjugate working solution was dispensed into each well. The plate was subsequently sealed and incubated statically at 37°C for 30 minutes. After this incubation period, the plate underwent five additional washes, each lasting one minute.Subsequently, 90 µL of 3,3’,5,5’-Tetramethylbenzidine [TMB] substrate solution was added, and then incubation continued for 20 minutes at 37°C. The process concluded with the addition of 50 µL of stop solution, after which the plate was analysed at 450 nm by a microplate reader (MultiSkan Sky, Thermo Scientific, USA).The serum levels of IL-6 in the samples wereextrapolated from a standard curve, correlating the concentration of the target cytokines with the OD450 values.

Statistical analysis

GraphPad Prism software (GraphPad Software Boston, USA) used for statistical analysis of the data. Categorical variables are reported as frequencies and percentages [n (%)]. Continuous variables were compared between paired groups using paired-samples *t*-tests. A two-tailed *p*-value of less than 0.05 was considered statistically significant.

3. Results:

A total of 71 women diagnosed with cervical neoplasia were included in the study, with the majority belonging to the 41-50 years age group, accounting for 23.84% of the participants. Additionally, 48 age-matched healthy controls were also part of the research. The study predominantly involved participants from rural areas, comprising 76.05% of the total population. Notably, 39.43% of the individuals reported a history of smoking.

The average age of patients diagnosed with cervical neoplasia was 51.03 years, with a standard deviation of 4.34 years, and ages varied between 18 and 76 years [Figure 1].

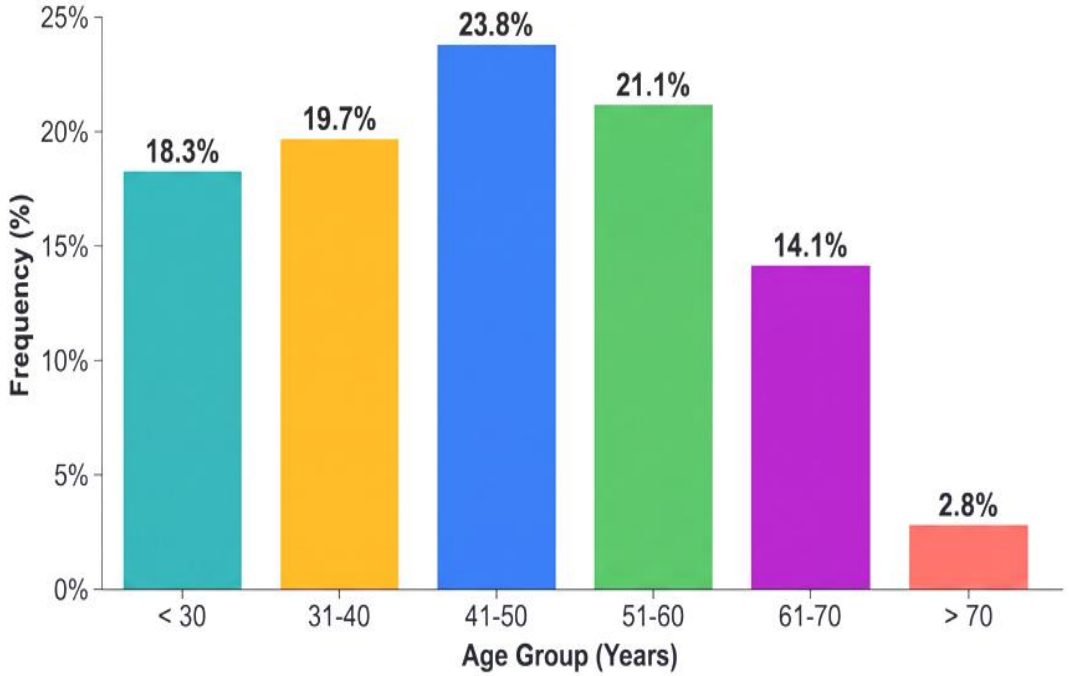

Figure 1. Age-specific presentation of patients with cervical neoplasia (n=71)

The majority of the subjects had experienced 1 to 2 pregnancies, accounting for 84.50%, while 15.49% indicated having more than three pregnancies. A detailed demographic profile is detailed in Table 1.

Table 1: Demographic and risk factors of the study participants (n=71)

Variables	**Frequency (%)**
Population distribution, n (%)	
Urban	17 (23.94%)
Rural	54 (76.05%)
Marital status, n (%)	
Unmarried	08 (11.26%)
Married	63 (88.73%)
Smoking, n (%)	
Smoking	28 (39.43%)
Non-smoking	43 (60.56%)
BMI (Kg/m^2), n (%)	
Normal (18.5-24.9)	26 (36.61%)
Overweight (25.0-29.9)	37 (52.11%)
Obesity (≥30.0)	08 (11.26%)
No. of pregnancies, n (%)	
1-2	60 (84.50%)
≥ 3	11 (15.49%)

Within the cervical neoplasia cohort, histological examination of 71 cases revealed that 17 cases, or 23.94%, were

diagnosed with invasive cancer.The serum IL-6 concentrations were significantly increased in individuals diagnosed with cervical neoplasia compared to the controls (p=0.001) group [Figure 2].

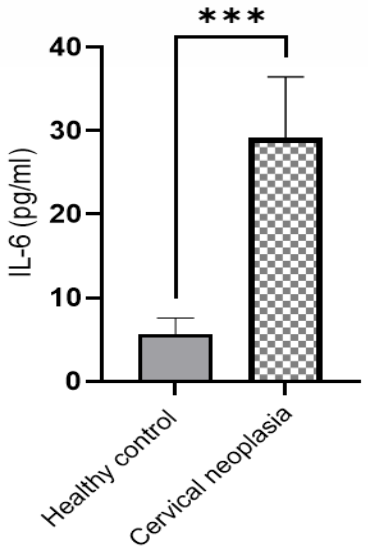

Figure 2: Serum interleukin -6 (IL-6)levelsin healthy controls and patients with cervical neoplasia

Interleukin-6 (IL-6) levels in patients with cervical neoplasia (n = 71) and controls (n = 48). Differences were considered statistically significant at $p < 0.05$ (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$).

4. Discussion

Cervical cancer persists as a major public health challenge and one of the most prevalent gynecological malignancies globally. Approximately 94% of cases occur in low- and middle-income countries, reflecting pronounced disparities in access to screening, early diagnosis, and therapeutic interventions [Chidebe et al., 2025]. Although cervical cancer is largely preventable and effectively manageable when identified at an early stage, it remains a critical public health challenge in India. Currently, it represents the second most prevalent malignancy among Indian women [Bhatla et al., 2021]. Persistent high-risk HPV infection can drive inflammation that contributes to cervical cancer progression. [zurHausen H, 2009].

Interleukin-6 (IL-6) is a key inflammatory cytokine in the tumor microenvironment, promoting cancer progression and treatment resistance Bharti R et al., 2016]. Inflammatory cytokines such as IL-6 may serve as biomarkers to assess disease stage, monitor treatment response, and inform targeted therapy. Regional data on inflammatory biomarker IL-6 expression in cervical neoplasia are limited. This study addresses this gap by quantifying serum IL-6 levels and evaluating their prognostic significance in patients with cervical neoplasia.

Cervical cancer shows pronounced geographic and socioeconomic disparities worldwide, with incidence rising as human development levels decline [Ou Y et al., 2025]. Lower socioeconomic status is associated with higher incidence, reduced screening, and poorer survival [Datta 2009, Singh et al., 2022]. In present study the majority of women presented from low socio economic class, from rural areas.

The host immune microenvironment is a critical determinant of cervical carcinogenesis and disease progression. Specifically, Bonin-Jacob et al. (2021) demonstrated significantly elevated concentrations of interleukin-6 (IL-6) in patients harboring high-risk human papillomavirus (HR-HPV) infections. This upregulation suggests that IL-6 contributes to an immunosuppressive milieu, potentially compromising natural killer (NK) cell cytotoxicity and

thereby facilitating sustained viral persistence [Bonin-Jacob et al., 2021]. In a landmark study, Wei et al. showed that IL-6 promotes cervical tumor growth in vivo by activating STAT3 and stimulating VEGF-dependent angiogenesis [Wei e al., 2003]. Moreover, Cheng et al. (2026) reported elevated serum IL-6 and IL-10 levels in patients with cervical cancer, suggesting that these cytokines may serve as biomarkers of disease progression [Cheng et al 2026].

In this study the levels of IL-6 levels were significantly higher in patients with cervical neoplasia than those observed in the control group. These findings align with Cai et al. (2022), who reported elevated serum IL-6 in patients with cervical cancer and linked it to unfavourable clinical features and poorer overall and disease-free survival [Cai et al 2022].. Adenekan et al. in 2025 also reported significantly higher serum IL-6 levels in women with cervical cancer compared with cancer-free counterparts. Cao et al. recently reported that detecting serum Th1/Th2 cytokine imbalance and elevated IL-6 and IL-10 levels can improve diagnostic accuracy in patients with HR-HPV-positive cervical cancer, providing valuable serological support for early identification of disease progression [Cao et al., 2026]. Elevated IL-6 may reflect suppression of tumour-specific immune responses, potentially contributing to disease progression [Adenekan et al.,2025].This study has a limitation, by its relatively small sample size; nevertheless, it provides valuable baseline information for the region. To enhance the reliability of these findings, further research with a larger sample size is warranted.

5.Conclusion:

The levels of IL-6 found in the patients were markedly elevated in cervical neoplasia subjects'compared to serum levels in the controls. Overall, the observation that elevated IL-6 levels and TNFα indicates a possible down-regulation of tumor-specific immune responses in cervical neoplasia, contributing to promote tumor progression. Further Additional research is required with a larger sample size to obtain a more comprehensive understanding of the findings.

Conflicts of Interest: None

Author Contributions: Experiments and analysis of data by SKP, JC, AD, BKB, RG, DP, ARKP study design and mentoring, SKP and ARKP wrote the manuscript, with all contributors having reviewed and approved the final version.

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