

# Detect the Levels of Some Cytokines in Women Infected With Human Papillomavirus in Kirkuk City

**Asmaa Jamal Mohammed**

Department of Biology, College of Science, University of Kirkuk, Iraq,  
asmaa.babani92@uokirkuk.edu.iq

**Wijdan Abdulghani Saleh Alhammadi**

Department of Biology, College of Science, University of Kirkuk, Iraq,  
wijdan.alhammdi@uokirkuk.edu.iq

**Zobaida Mahmood Salih**

Department of Biology, College of Education for Pure Science, University of Mousl. Iraq,  
Zubaida.altayi@uomosul.edu.iq

**Parzhin Sardar Mohammed**

Department of Biology, College of Science, University of Kirkuk, Iraq

---

**Received:** 2024, 26, May

**Accepted:** 2025, 27 Jun

**Published:** 2025, 28 Jul

Copyright © 2025 by author(s) and Bio Science Academic Publishing. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).  
<http://creativecommons.org/licenses/by/4.0/>



Open Access

**Annotation: Background & aim:** The most frequent cause of cutaneous warts and mucosal papillomas is the human papillomavirus (HPV), and high-risk strains of the virus are linked to the development of colorectal, genital, and oropharyngeal cancers. Therefore, the current study aims to detect the levels of some physiological parameters and cytokines in women infected with human papillomavirus.

**Materials & methods:** The study was conducted at the Department of Biology, College of Sciences, University of Kirkuk. The sample included (240) Iraqi women patients with cervical diseases who attended Kirkuk Teaching Hospital and private clinical in Kirkuk City from February to June 2025.

**Results:** by using ELISA, it was found that the number of infected women was 37 (15.4%) out

---

of a total of 240. The highest infection rate was found in the 20-30 age group, reaching 51.4%, while the lowest infection rate was in the 41-50 age group, reaching 13.5%. The average age of women was  $33.7 \pm 13.29$ . The findings exhibited the levels of some cytokines in HVP patients and healthy women, where IL-10 levels in serum of HVP patients ( $2.93 \pm 0.46$ ) demonstrated significant ( $P < 0.05$ ) elevated compared with control women ( $1.84 \pm 0.17$ ). the levels of IL-17 exhibited a significant ( $P < 0.05$ ) elevated in HVP patients ( $254.3 \pm 25.91$ ) compared with healthy women ( $165.1 \pm 15.08$ ). the levels of tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) exhibited significant ( $P < 0.05$ ) elevated in HVP patients ( $3.04 \pm 0.53$ ) compared with healthy women ( $1.63 \pm 0.21$ ).

**Conclusions:** The younger women are more susceptible to HPV infection than other age groups, and that HPV infection directly affects the levels of certain cytokines that play an important role in infection.

**Keywords:** HVP, cytokines, interleukins, tumor necrosis factor, IL-17.

---

## Introduction

Sexually transmitted diseases such genital warts and cervical, anal, and oropharyngeal cancers have been linked to the human papillomavirus (HPV). Of the more than 150 HPV genotypes, 13 have been linked to cervical cancer, with HPV genotypes 16 and 18 responsible for 50–60% of instances of cervical intraepithelial neoplasia 2+ (CIN 2+) and 66% of all cervical cancer cases [1, 2]. Although HPV infection is common, it is preventable. Of all the different types of HPV infection, genital HPV is the most common form that is spread through sexual contact. Age at first sexual contact and the number of sexual partners are major factors in many genital HPV infections. In a study they did, Bosch F X et al. also reported this, noting that the HPV-DNA of genital type increases in both males and girls when the number of sexual partners increases and the first sexual encounter occurs at a younger age [3, 4]. The first host response is dependent on tissue-innate immune components like myeloperoxidase (MPO) and mucosal lactoferrin (LF), and it plays a role in the intercellular route of malignant cells that is triggered by apoptosis [5, 6]. The natural course of HPV infection of the uterine cervix is probably influenced by local immune responses. An essential regulator of HPV transcription is cytokines [7]. The two primary categories of cytokines in immune responses to infection are immunostimulating T helper 1 (Th1)-type cytokines and T helper 2 (Th2)-type cytokines. Th1-type cytokines, such as interferon  $\gamma$  and TNF- $\alpha$ , largely promote cell-mediated immunity, whereas Th2-type cytokines, such as interleukin-6 (IL-6) and IL-10, primarily generate humoral immunity and are immunoinhibitory for cell-mediated responses [8]. Cytokines are crucial for the immune system's fight against HPV infection because they influence viral replication and divide the immune system into Th1 and Th2 patterns [9]. Viral clearance and inflammatory responses are significantly influenced by TNF- $\alpha$  [10]. A significant factor in a successful Th1-type cellular

immune response against HPV infection is IFN- $\gamma$ , which is released by Th1 cells, cytotoxic T cells, and activated natural killer cells [11]. Persistent HPV infection and HPV-related neoplasia development may be linked to defective IFN- $\gamma$  production [12]. On the other hand, IL-6 and oncogenic HPV infection might work in concert [13]. As cytokine expression in the cervical milieu shifts, IL-10 may promote the persistence and advancement of HPV-related lesions under dysplastic development [14]. Therefore, the current study aims to detect the levels of some physiological parameters and cytokines in women infected with human papillomavirus.

### Materials & methods

The study was conducted at the Department of Biology, College of Sciences, University of Kirkuk. The sample included (240) Iraqi women patients with cervical diseases who attended Kirkuk Teaching Hospital and private clinical in Kirkuk City from February to June 2025. The women who took part were informed about the study in their native tongue, and their written and informed consent was acquired. Samples of blood were drawn from the vein, and serum was extracted following centrifugation in accordance with standard protocol.

### Inclusion criteria

The participants were married, sexually active, between the ages of 20 and 50, not pregnant, and had never undergone a hysterectomy. These women arrived at OPD with symptoms of infections, including post-coitus bleeding, intermittent bleeding, contact bleeding, vaginal discharge, genital itching, and dyspareunia.

### Exclusion criteria

The participants were vaccinated, pregnant, sexually naïve, had undergone hysterectomies, and had cervical cancer. Women who did not wish to participate were also excluded.

### Measurements

- Human papillomavirus-16 (HPV-16): ELISA Kit (SUNLONG, China) uses Sandwich-ELISA to measure HPV-16 in human serum and plasma.
- Intetlukin-1 beta (IL-10): ELISA Kit (SUNLONG, China) uses Sandwich-ELISA to measure IL-10 in human serum and plasma.
- Intetlukin-17 (IL-17): ELISA Kit (SUNLONG, China) uses Sandwich-ELISA to measure IL-17 in human serum and plasma.
- Tumor Necrosis Factor- $\alpha$  (TNF- $\alpha$ ): ELISA Kit (SUNLONG, China) uses Sandwich-ELISA to measure TNF- $\alpha$  in human serum and plasma.

### Statistical analysis

SPSS 26.0 for Windows (Chicago, IL, USA) was used to gather, tabulate, and perform statistical analysis on the data. Statistical significance (S) is defined as  $p < 0.05$ , whereas statistical non-significant (NS) is defined as  $p \geq 0.05$  [15, 16].

### Results & Discussion

Table 1 shows the prevalence of HVP16 among women with cervical inflammation. Using ELISA, it was found that the number of infected women was 37 (15.4%) out of a total of 240, while the negative results were 203 (84.6%).

**Table 1. Prevalence of HVP16**

Type	+ve results	-ve results	Total	P value
HVP6	37(15.4%)	203(84.6%)	240	0.001

According to the results of our prospective study, the community as a whole had a 15.4% HPV16 prevalence, with the largest percentage occurring in people with high grade lesions (HSIL). Infection rates were considerably greater among those who used natural contraceptives than among those who used other methods, and half of the individuals with a history of gonococcal infection tested positive for HPV-16. A 2009 study in Melbourne, Australia, found a higher prevalence, showing that one of the high-risk HPV infections was present in 83.9% of women having an abnormal pap smear [17]. However, a different study conducted in Turkey revealed that the general HPV prevalence in women with abnormal pap smears was 36%, with HPV 16 infection being the most prevalent [18]. Although it was not statistically significant, the highest HPV frequency was found in people under 35 years. Women under 30 years old had a higher risk of HPV infection, according to a UK study [19]. The second population group (UK) may have received an earlier diagnosis and intervention, which could account for the discrepancy between the two results.

Table 2 shows the prevalence of HVP16 according to age of women with cervical inflammation. The highest infection rate was found in the 20-30 age group, reaching 51.4%, while the lowest infection rate was in the 41-50 age group, reaching 13.5%. The average age of women was  $33.7 \pm 13.29$ .

**Table 2 shows the prevalence of HVP16 according to age of women**

Age (years)	No.	%
20-30	19	51.4%
31-40	13	35.1%
41-50	5	13.5%
Total	37	100.0%

Because younger women were thought to be more sexually exposed and to have several partners, their prevalence was higher [20, 21]. Similar to many previous findings, the HPV infection age-specific pattern displayed a bimodal infection peak. Shortly after sexual beginning, HPV infection at a younger age peaks [22]. As a result of their immature transformation zone, women in their twenties and thirties are particularly vulnerable to HPV infection (Xu et al. Although they may still test positive for HPV DNA, women 30 years of age or older who possess a mature, stable transformation area are less likely to get infected with HPV again because of their long-standing, continuous infection from the past that has not been immunely eliminated [23]. Similarly, HPV infection rates in the Chinese population ranged from 17.7 to 41.8% for each age group. Women under the age of 20 had the highest frequency of HPV infection, with an infection rate of 41.8%, followed by those over 60 with an infection rate of 22.9% and those between 20 and 29 with an infection rate of 21.1% [24]. As opposed to the current study, a population-based survey conducted in Bangladesh revealed that the age-specific prevalence first declined for the 25–34 age group, then rose for the 35–44 age group, and finally declined for the over-45 age group [25]. According to estimates, by the time they are 50 years old, over 80% of sexually active women will have contracted genital HPV. In the Uttarakhand population, the age-wise distribution revealed high-risk positive of 15.21% in the 15–35 age group, which is comparable to our findings [26]. Women over 55 who started having intercourse at a young age were more likely to contract HPV, according to Kadian LK et al. [27]. By using particular genotype information, this age variance is important for rationalizing the recently proposed screening programs and patient management protocols [21, 28].

Table (2) show the levels of some cytokines in HVP patients and healthy women, where IL-10 levels in serum of HVP patients ( $2.93 \pm 0.46$ ) demonstrated significant ( $P < 0.05$ ) elevated compared with control women ( $1.84 \pm 0.17$ ), as shown in figure (1). the levels of IL-17 exhibited a significant ( $P < 0.05$ ) elevated in HVP patients ( $254.3 \pm 25.91$ ) compared with healthy women ( $165.1 \pm 15.08$ ), as shown in figure (2). the levels of TNF- $\alpha$  exhibited significant ( $P < 0.05$ ) elevated in HVP patients ( $3.04 \pm 0.53$ ) compared with healthy women ( $1.63 \pm 0.21$ ), as shown in figure (3).

**Table (2): the levels of some cytokines in studied groups**

Groups Parameter	Control (50)	HVP (37)	P-Value
IL-10 (ng/ml)	$1.84 \pm 0.17$	$2.93 \pm 0.46$	0.001
IL-17 (pg/l)	$165.1 \pm 15.08$	$254.3 \pm 25.91$	0.001
TNF- $\alpha$ (ng/ml)	$1.63 \pm 0.21$	$3.04 \pm 0.53$	0.001

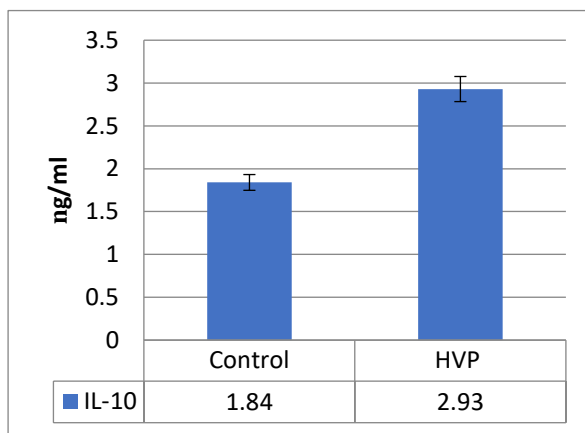


Figure (1): IL-10 levels in patients and control.

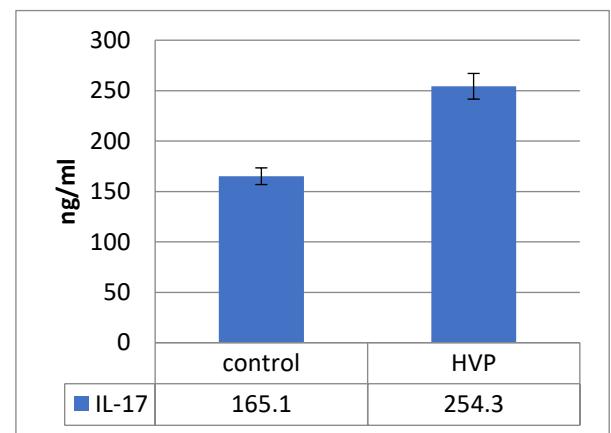


Figure (2): IL-17 levels in patients and control.

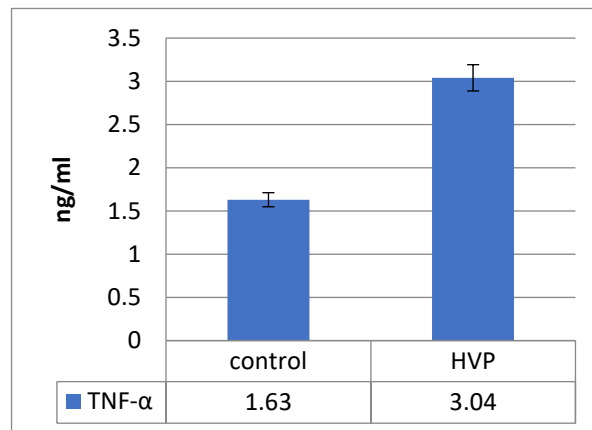


Figure (3): TNF- $\alpha$  levels in patients and control.

The results showed that, in comparison to healthy people, patients had higher average levels of TNF $\alpha$  and IL-10. Similar changes in cytokine expression were reported by Alazawy et al. in a study on immune responses in patients with cervical cancer in Hawler City, Iraq [29]. Similar to the results of our study, theirs also showed that the participants had considerably higher levels of TNF $\alpha$  and IL-10. While the Human Papillomavirus (HPV) is undoubtedly a significant contributor to the development of cervical cancer, it is important to recognize that squamous intraepithelial lesions, which may or may not progress to cervical cancer, are also influenced by other variables. In this context, one important anti-inflammatory factor that promotes immunosuppression and aids in immune system evasion is interleukin 10 (IL-10) [30]. Although

its exact function in cancer is still up for debate, IL-10 appears to rise in tandem with the development of SIL and is even more prevalent in cervical malignancies. The progression of HPV infection to SIL or cervical cancer may be aided by the cycle that favors an immunosuppressive milieu in the cervix due to the interaction between HPV and IL10 [31]. One cytokine that has both anti-tumor and tumor-promoting properties is TNF- $\alpha$ . Although it has immune-boosting, antiviral, and anticancer effects, it has also been linked to tumor growth. TNF- $\alpha$  secreted by tumor tissue can accelerate the initiation and progression of cancer, induce angiogenesis, and encourage the proliferation of tumor cells [32]. In line with our findings, Li et al. [33] came to the conclusion that HPV infection increases the release of IL-17 by activating the signal transducer and activator of the transcription 3 pathway (Stat3). This is in line with the positive feedback loop theory, which holds that HPV causes the release of IL-17, which in turn promotes viral replication and keratinocyte proliferation [34]. Similarly, the mean serum IL-17 levels in the case group were  $141.1 \pm 155.5$  pg/ml and the control group were  $49.97 \pm 22.36$  pg/ml, with a significant difference ( $p < 0.001$ ), according to Alkady et al. [35]. Compared to the control group, the cases group's mean IL-17 was noticeably greater. In contrast to our research, they found a non-significant negative connection ( $p > 0.05$ ) between the number of lesions and their duration with IL-17. Moreover, by disrupting cytolytic T-cell function, IL-17 prevents efficient antiviral response and prolongs viral infection. This feedback loop, which is regulated by IL-17, encourages viral persistence during viral infection, which aids in the pathophysiology of virus-induced chronic illness [35]. We can therefore draw the conclusion that IL17-mediated viral persistence and viral-induced IL17 production are part of a vicious cycle. The link between HPV infection and elevated IL-17 levels is clearly supported by a recent trial in which patients who received secukinumab for several months saw a significant reduction in cutaneous HPV lesions [36].

## Conclusions

The results of the current study showed that younger women are more susceptible to HPV infection than other age groups, and that HPV infection directly affects the levels of certain cytokines that play an important role in infection.

## References

1. Saadoon I. H., Al-Zahraa M. S. The Prevalence of Human Papilloma Virus among Breast Cancer Women in Relation with IL-8 Level in Kirkuk Province. *Kirkuk University Journal /Scientific Studies (KUJSS)*. 2018; 13(1): 118 -130.
2. Eric F., Ozdemir E., Khalil P., Meaghan B., Aidan P. A Review of Human Papillomavirus Vaccination and Associated Ethical Concerns. *Infect Chemother*. 2024; 56(4):432-439.
3. Singh S, Ahmad S, Srivastava AN, Misra JS. A Review on Role of Human Papilloma Virus (HPV) in Health-Related Diseases. *Adv. Med. Dental Health Sci*. 2020; 3(3):34-40.
4. Milano G., Giovanni G., Nicola N., Emanuele M., Ilaria M. Human Papillomavirus Epidemiology and Prevention: Is There Still a Gender Gap?. *Vaccines (Basel)*. 2023; 11(6):1060.
5. Gardella B, Iacobone AD, Musacchi V, Calvino IG, De Amici M, Torre C, Bogliolo S, Spinillo A. The Mucosal Innate Immune Response in Primary Human Papillomavirus Infection: A Pilot Study. *J. Low. Genit. Tract Dis*. 2016; 20, 338–342.
6. Gardella B., Mattia D., Giulia V. C., Valentina M., Mara D., Arsenio S. Cytokines and chemokines levels in primary HPV infection: a pilot study. *Acta virologica*. 2021; 65: 75 – 81.
7. Sellors J.W. et al. Prevalence and predictors of human papillomavirus infection in women in Ontario, Canada. Survey of HPV in Ontario Women (SHOW) Group *CMAJ*. 2000;



8. Munoz N. et al. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *N. Engl. J. Med.* 2003;
9. Barros M. R., Talita H. A., Cristiane M., Aldo V., Antonio C. F. Viral Modulation of TLRs and Cytokines and the Related Immunotherapies for HPV-Associated Cancers. *J Immunol Res.* 2018; 2018:2912671.
10. Zawawi Z. M., Jeevanathan K., Rozainanee M. Z., Ravindran T., Dayang F. B., Wei B. Y. Prospective Roles of Tumor Necrosis Factor-Alpha (TNF- $\alpha$ ) in COVID-19: Prognosis, Therapeutic and Management. *Int J Mol Sci.* 2023; 24(7):6142.
11. Mohammed M. M., Zaytoon A. I., Nadia M. An exploration of the natural and acquired immunological mechanisms to high-risk human papillomavirus infection and unmasking immune escape in cervical cancer: A concise synopsis. *Tzu Chi Med J.* 2024; 37(1):28–41.
12. Zhang Y., Ke Q., Jianjun R., Yu Z., Ping C. Roles of human papillomavirus in cancers: oncogenic mechanisms and clinical use. *Signal Transduction and Targeted Therapy.* 2025; 10(44): 1-7.
13. Matei C., Laura S. D., Mircea T. Interleukins in the Pathogenesis of Warts: Insight from the Last Decade—A Narrative Review. *J Clin Med.* 2025; 14(6):2057.
14. Torres-Poveda K., Margarita B., Claudia M., Ana I B., Víctor Hugo B., Oscar P., Vicente M. Role of IL-10 and TGF- $\beta$ 1 in local immunosuppression in HPV-associated cervical neoplasia. *World J Clin Oncol.* 2014; 5(4):753–763.
15. Saleh A.H., Aldulaimi L.H., Ahmed N.M. Potential of nanoemulsion of spiramycin in alleviating histological and embryonic changes in Swiss albino mice infected with congenital toxoplasmosis. *Journal of Applied and Natural Science,* 2024; 16(4): 1842–1848.
16. Mohammed S.H., Saleh A.H., Abu-Elteen K.H., Dheeb B.I., Abdulateef S.M. Role of Fluconazole Nanoemulsion in Inhibiting Liver Candidiasis in Female Mice and their Embryos. *Jordan Journal of Biological Sciences,* 2025; 18(1): 173–180
17. Stevens MP, Garland SM, Tan JH, Quinn MA, Petersen RW, Tabrizi SN. HPV genotype prevalence in women with abnormal pap smears in Melbourne, Australia. *J Med Virol* 2009; 81(7):1283–91.
18. Dursun P, Senger S, Arsalan H, Kuscu E, Ayhan A. Human papillomavirus (HPV) prevalence and types among Turkish women at a gynecology outpatient unit. *BMC Infectious Diseases* 2009; 9:191.
19. Sargent A, Bailey A, Almonte M, Turner A, Thomson V, Pito J, et al. Prevalence of type specific HPV infection by age and grade of cervical cytology. *British journal of cancer. Br J Cancer* 2008; 98(10):1704–9.
20. Getinet M, Gelaw B, Sisay A, Mahmoud EA, Assefa A. Prevalence and predictors of Pap smear cervical epithelial cell abnormality among HIV-positive and negative women attending gynecological examination in cervical cancer screening center at Debre Markos referral hospital, East Gojjam, Northwest Ethiopia. *BMC Clin Pathol.* 2015; 15:16
21. Kulkarni Sayali P, Paliwal S., Kosta Susmit. Genotypic Diversity of Human Papilloma Virus (HPV) types and its prevalence with cervical cancer in Central India. *Cureus.* 2023; 15(2); e35227.
22. Baloch Z., Li Y, Yuan T, Feng Y, et al. Epidemiologic characterization of human papillomavirus (HPV) infection in various regions of Yunnan Province of China. *BMC Infect Dis.* 2016; 16:228.

23. XuY, DottoJ, HuiY,etal.High grade cervical intraepithelial neoplasia and viral load of high-risk human papillomavirus: significant correlations in patients of 22 years old or younger. *Int J Clin ExpPathol*. 2009;2(2):169–175
24. Xiangpeng Wang<sup>1</sup> , Yuan Song<sup>1</sup> , Xiaofei Wei<sup>1</sup> , Guanyu Wang<sup>1,2</sup>, Ruili Sun<sup>1\*</sup>, Mingyong Wang<sup>1\*</sup> and Lijun Zhao. Prevalence anddistribution ofhuman papillomavirus genotypes amongwomen attending gynecology clinics innorthern Henan Province ofChina. *Virology Journal* (2022) 19:6
25. Nahar Q, Sultana F, Alam A, Islam JY, Rahman M, Khatun F, et al. Genital human papillomavirus infection among women in Bangladesh: findings from a population-based survey. *PLoS One*. 2014;9(10):e107675
26. Sharma, N.; Sharma, V.; Singh, P.R.; Kushwaha, R.S.; Nautiyal, S.C.; Sailwal, S.; Singh, R.K.; Masood, T.; Mishra, P.; Singh, R.K. Age wise distribution of high risk Human Papillomavirus in Northern Indian women. 2012.
27. Kadian LK, Singhal G., Sharma S, Chauhan P, Nanda S, Yadav R. Incidence and Association of HPV16 and 18 with Various Risk Factors in Cervical Cancer Patients in Population of Haryana Region, India.*Journal of Clinical and Diagnostic Research*. 2019 Feb, Vol-13(2): QC10-QC13.
28. Deksissa ZM, Tesfamichael FA, Ferede HA.Prevalence and factors associated with VIA positive result among clients screened at Family Guidance Association of Ethiopia, southwest area office, Jimma model clinic, Jimma, Ethiopia 2013: a cross-sectional study. *BMC Res Notes*.2015;8:618
29. Alazawy A.K., Arshad S.S., Hair-Bejo M., Omar A.R., Sharif S., Hafidz M.A.I. Isolation and adaptation of feline coronavirus in crandell feline kidney (CRFK) cell culture. 21st Veterinary Association Malaysia Congress, 2009; 7-9, The Legend, Water Chalets, Port Dickson, Negeri Sembilan.
30. Ali K. S., Ali H. Y., Jubrael J. M. Concentration levels of IL-10 and TNF  $\alpha$  cytokines in patients with human papilloma virus (HPV) DNA+ and DNA– cervical lesions. *Journal of immunotoxicology*, 2012; 9(2), 168- 172.
31. Bautista-Valarezo E., Vega Crespo B., Maldonado-Rengel R., Espinosa M. E., Neira V. A., Verhoeven V. Knowledge and perceptions about cervical cancer and HPV screening in women in rural areas of Ecuador: a qualitative research study. *International Journal of Environmental Research and Public Health*, 2022; 19(17), 11053.
32. Mahmoud M. M., Rifat A. G. Relation of Human Papilloma Virus Infection with Pre Malignant and Malignant Endometrial Lesions. *Prof.(Dr) RK Sharma*, 2021; 21(1), 490.
33. Li YX, Zhang L, Simayi D, Zhang N, Tao L, Yang L, et al. Human papillomavirus infection correlates with inflammatory Stat3 signaling activity and IL-17 level in patients with colorectal cancer. *PLoS One*. 2015;10(2): e0118391.
34. Brunet-Possenti F, Charpentier C, Collin G, Descamps D, Descamps V. Impact of antiinterleukin-17 treatment on cutaneous and genital human papillomavirus infection. *Br J Dermatol*. 2018;179(5):1179-80.
35. Alkady O, Abduulah S, Ismail Y, Rezk S. Evaluation of Interleukin-17 in Viral Warts. *Benha Medical Journal*. 2021;38(1):94-101.
36. Chiu H-Y, Tsai T-F. The impact of secukinumab treatment on the prevalence of human papillomavirus in patients with psoriasis: A pilot study. *J Am Acad Dermatol*. 2016;75(1):224-6.