ORIGINAL ARTICLE

Serum Level of IL22 and IL17 in Recalcitrant Common Warts

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ABSTRACT

Background: *Recalcitrant warts are defined as warts persistent for longer than two years in spite of proper use of appropriate treatment. The interleukin-17 (IL-17) family cytokines have an essential protective role in host immune response to infection. IL-22 production is upregulated by NK and CD4 + T cells secondary to different types of viral infections throughout which IL-22 causes an essential role in the antiviral defense mechanism.* ***Objectives:*** *The aim of this study was to measure the level of IL-22 and Il-17 in recalcitrant common warts and healthy controls in an attempt to explain their role in wart pathogenesis.* ***Methodology:*** *This was a case control study conducted on 50 patients with recalcitrant warts, and 40 healthy controls. All cases were subjected to history taking, physical examination and laboratory investigations comprising serum IL22 and IL 17 levels.* ***Results:*** *Cases showed significantly lower IL-17 and IL22 levels in comparison with the control group. ($p<0.001$). Moderate accuracy was found for IL22 and IL17 to discriminate between cases and control groups. In addition, both IL-17 and IL-22 could be used for prediction of recalcitrant warts susceptibility ($p<0.001$).* ***Conclusion:*** *Cases with recalcitrant warts were associated with significant decreases in serum IL-22 level, and this low level may have a potential function in improving the cell-mediated immune response towards HPV infections. Patients with recalcitrant warts were associated with significant reductions in serum IL-17 value; IL-17 deficiency plays a main role in recalcitrant wart pathogenesis via disturbance of the balance of the immune system and deficiency of immune cells. As a result, IL-17 may have an essential role in the antiviral immune response to HPV infection.*

INTRODUCTION

Viral warts are frequent lesions that cause the proliferation of keratinocytes and mucous membranes. It is caused by HPV and it is acquired from direct contact with infected patients or from environment[1].

Recalcitrant warts could be described as warts persistent for longer than 24 months in spite of treatment including cryotherapy with liquid nitrogen, curettage, excision, electrosurgery or laser treatment. It is characterized by being formerly subjected to at least two conventional therapeutic approaches but didn't respond or they had frequently acquired clinical manifestations for longer than 24 months and it is extensive, periungual or subungual [2].

HPV in nearly all patients is self-limited and could be eradicated by humoral and cell mediated immunity[3]. It mainly reliant on intact cellular immunity comprising NK [4] and cytotoxic T cells [5]. It is believed that Th-1 cytokines IL-2, INF-γ, and TNF-a and IL-17 are comprised in HPV clearance. Deficits in cell-mediated immunity or the disproportion between Th1 and Th2 might be associated with recalcitrant warts or the development of HPV-accompanying tumours [4]. It is still partially identified why there is evident failure of the immunity in otherwise healthy subjects to eradicate warts for years [6].

IL-17 and IL-22 have main functions in host defense against microorganisms as well as in the development of chronic inflammatory disorders [7]. IL-17 mostly causes inflammatory tissue responses and it is comprised in the pathogenesis of a lot of autoimmune disorders, while IL-22 is mainly protective and regenerative[8].

The aim of this Work is to assess the levels of IL-22 and Il-17 in recalcitrant common warts and healthy controls in attempt to explain their role in common wart pathogenesis.

METHODOLOGY

This was a case study conducted within a duration of one year from 2021 to 2022 on two groups; **Group I** was composed of 50 patients with recalcitrant warts who were recruited from the Outpatient Clinic of Dermatology, Andrology and STDs Department, Mansoura University Hospitals. **Group II** was composed of 40 healthy participants as a control group.

***Inclusion criteria*:**

Patients' Age >12 years, both sexes, with recalcitrant and ordinary common warts of different size, with multiple veruccae vulgaris resistant to treatment (they failed to show any response to at least one destructive mode of treatment, with multiple veruccae vulgaris that were relapsed at least once after treatment .

***Exclusion criteria*:**

Patients' Age <12 years old, who were suffering from another dermatological disease, with acute febrile illness, past history of asthma, allergic skin disorders, a history or clinical evidence of acute or chronic infection, concomitant treatment of warts, associated intake of immunosuppressive medications, other comorbidities like DM, hypertension, renal diseases or cardiac diseases, pregnant and breastfeeding, heavy smokers, with immunosuppressive diseases or on immunosuppressant or immune modulatory drugs, having any active malignant tumour or are undergoing therapy for malignant tumours (except non-melanoma skin cancer), who are insane, unable to give written informed consent.

***Methods*:**

All cases were subjected to full history taking which included age, sex, occupation, residence, special habits, marital status, systemic diseases, past history of medical disease, present history which included onset, course, duration, site, numbers of warts and history of recurrence, family history of any similar conditions. In addition, full general clinical examination was conducted which included BMI (Wight (kg/height^2 (m))).

Patients with warts were examined locally for: site, number, shape of lesions, and presence of inflammation. Types and sites of warts, activity of any new lesions, interval warts and presence of 2ry bacterial infections were assessed. The diagnosis of warts was confirmed by the examiner by presence of firm papules or endophytic growth. History taking and dermatologic assessment were conducted for all cases comprising the nail, oral and nasal mucosa, perianal region and genitalia to detect wart duration, numbers, affected area, and types, and whether the warts occurred for the 1st time or were recurrent following a preceding management. Each blood sample was divided into 2 tubes: 4 milliliter of blood was given into a collection tube. Blood was allowed to clot before being centrifuged for ten min at 3000 r.p.m, and serum was collected for clinical chemistry tests, CRP, the IL17 and IL22 assays (ELISA kit is Sandwich-ELISA). One milliliter destructive modalities

Five mm of venous blood had been drawn from all studied subjects and supplied into a tri-potassium ethylenediaminotetraacetate (K3-EDTA) tube for CBC analysis. Serum was collected in serum gel tubes for other laboratory parameters.

Investigations:

Complete blood picture, urea and serum creatinine, ALT and AST,blood glucose level, CRP, assay of serum IL22 and IL 17 levels using Enzyme Linked Immunosorbent Assay method with commercial kit.

Ethical considerations:

Study design was approved by Institution Research Board of Mansoura Medical College with code no. **MS.21.09.1665**. Confidentiality was respected. Collected data weren't used for any other purposes. An informed written consent was acquired from all subjects.

Statistical analysis:

The collected data were revised, coded, and tabulated using SPSS **(IBM Corp, Version 25.0).** Data were analyzed based on the type of the acquired data. Mean±SD, median, standard error (±SE), and range were used for numerical data. Frequency and percentage were used for non-numerical data.

Student T Test was utilized for assessment of the significance of the difference between two groups. **Mann Whitney Test** was utilized for assessment of the significance of the difference of a non-parametric variable. **Chi-Square test** was utilized to evaluate the relation between two qualitative variables. **Correlation analysis** was utilized to the evaluate strength of relation between two quantitative variables. The ROC Curve offers a helpful method to properly assess the Sn and Sp for quantitative diagnostic measures.

Logistic regression analysis was utilized for the prediction of predisposing factors when the dependent variable is categorical. A p value is considered significant if <0.05.

RESULTS

Table (1) displays a comparison of demographic data among patients with recalcitrant warts and control group. The mean age of was 30.6 ± 8.70, ranged from 16 to 47 years. They were 27 male (54%) and 23 female (46%.) While mean age of control group was 31.65 ± 8.55, ranged from 18 to 47 years. They were 22 male (55%) and 18 female (45%), with non-significant differences between both groups concerning age and gender.

Table 1: Comparison of demographic data between both groups

	Cases n = 50		**Control n = 40**		**Test**	**P**
Age (years)						
Mean±SD.	30.60 ± 8.70		31.65 ± 8.55		t= 0.573	0.568
Median	28.0		31.50			
Min-Max	16.0 – 47.0		18.0 – 47.0			
Sex	***No.***	***%***	***No.***	***%***		
Male	27	54.0	22	55.0	X^2= 0.009	0.925
Female	23	46.0	18	45.0		

t: Student t test, X^2: Chi-Square, P: Comparing patients and control, *: Significant when p<0.05.

Table (2): shows that regarding onset, 45 case (90%) had chronic onset, while 5 cases (10%) had acute onset. Mean disease duration was 4.76 ± 0.97 months, median disease duration ranged () 1-36 months. All cases (100%) had progressive course, and multiple warts. Affected sites included face in 22 case (44%), arms in 21 case (42%), feet in 21 case (42%), hand in 16 cases (32%), neck in 9 cases (18%), fingers in 3 cases (6%), toes in 3cases (6%) , others in 4 cases (8%)

Table 2: **Clinical features among case group**

	Patients (n = 50)	
	No.	***%***
Onset		
Chronic	45	90.0
Acute	5	10.0
Course		
Progressive	50	100.0
Duration (months)		
Mean ± SE.	4.76 ± 0.97	
Median (Min. – Max.)	3.0 (1.0 – 36.0)	
Number		
Multiple	50	100.0
Site		
Face	22	44.0
Arms	21	42.0
Feet	21	42.0
Hand	16	32.0
Neck	9	18.0
Fingers	3	6.0
Toes	3	6.0
Others (legs, chest…etc.)	4	8.0

Table (3) shows that median IL22 in cases was 13.63 and ranged from 1.67 to 48.41, while in control group it was 41.26 ranged from 11.01 to 93.86. Cases group showed a statistically significant lower IL22 level when compared to control group (p<0.001).

Median IL17 in the cases was 27.12, ranged from 2.16 to 115.1, in control group it was 80.93 ranged from 22.21 to 189.1. Cases group revealed a significant lower IL17 level compared to controls (p<0.001). Mean IL22 in cases was 16.52 ± 1.64, ranged from 1.67 to 48.41, while in control group it was 41.97 ± 2.86 ranged from 11.01 to 93.86. Cases group showed a significant lower IL22 level when compared to controls (p<0.001). Mean IL17 in cases was 33.69 ± 3.45, ranged from 2.16 to 115.1, in control group it was 82.17 ± 5.68 ranged from 22.21 to 189.1. Cases group showed a statistically significant lower IL17 level when compared to controls (p<0.001).

Table 3: Comparison of serum IL22 and IL 17 levels between both groups

	Cases n = 50	Control n = 40	Test	P
IL22				
Mean ± SE.	16.52 ± 1.64	41.97 ± 2.86	U= 1779.0	<0.001*
Median	13.63	41.26		
Min. – Max.	1.67 – 48.41	11.01 – 93.86		
IL17				
Mean ± SE.	33.69 ± 3.45	82.17 ± 5.68	U= 1768.0	<0.001*
Median	27.12	80.93		
Min. – Max.	2.16 – 115.1	22.21 – 189.1		

SE: Standard error, Min.: Minimum, Max.: Maximum, U: Mann-Whitney. P: Comparing patients and control, *: Significant when p<0.05.

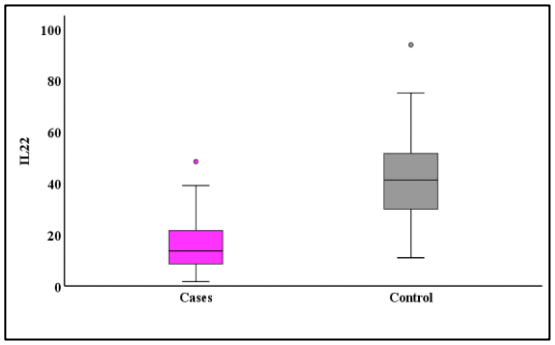

Fig. 1: Boxplot to compare serum IL22 levels among cases and control group.

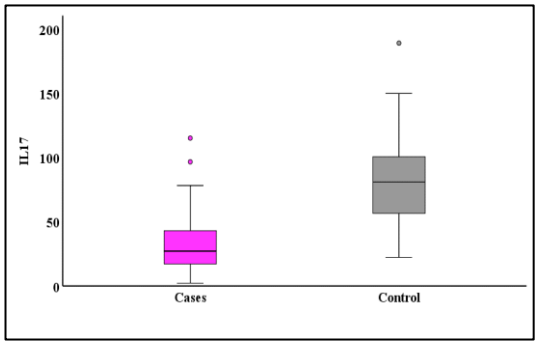

Fig. 2: Boxplot to compare serum IL 17 levels among cases and control group

Table (4) showed a non-statistically significant association between IL22, IL17 and smoking among cases group.

Table 4: Association between IL22, IL17 and smoking among cases group

	IL22			Test	P
	Mean ± SE.	Median	Min. – Max.		
Smoking					
Negative, (n=47)(94%)	15.69 ± 1.64	12.76	1.67 – 48.41	U= 116.0	0.065
Positive, (n=3)(6%)	29.52 ± 6.50	33.62	16.79 – 38.15		
	IL17			**Test**	**P**
	Mean ± SE.	**Median**	**Min. – Max.**		
Smoking					
Negative, (n=47)(94%)	32.08 ± 3.47	25.39	2.16 – 115.11	U= 117.0	0.059
Positive, (n=3)(6%)	58.88 ± 13.08	67.01	33.29 – 76.35		

SE: Standard error, Min.: Minimum, Max.: Maximum, U: Mann-Whitney.
P: Comparing the different categories. *: Significant when p<0.05.

Table (5) shows a non-statistically significant association between IL22, IL17and FH among cases group.

Table 5: Association between IL22, IL17 and family history among cases group

	IL22			Test	P
	Mean ± SE.	Median	Min. – Max.		
Family history					
Negative, (n=4)(8%)	21.34 ± 4.83	24.49	17.26 – 39.11	U= 123.0	0.210
Positive, (n=46)(92%)	25.23 ± 1.61	22.65	1.67 – 48.41		
	IL17			**Test**	**P**
	Mean ± SE.	**Median**	**Min. – Max.**		
Family history					
Negative, (n=4)(8%)	52.52 ± 9.67	58.78	34.35 – 78.18	U= 122.0	0.238
Positive, (n=46)(92%)	41.18 ± 3.43	45.22	2.16 – 115.11		

SE: Standard error, Min.: Minimum, Max.: Maximum, U: Mann-Whitney.
P: Comparing the different categories. *: Significant when p<0.05.

Table (6) shows a statistically significant higher level of IL-17 in patients with positive past history of recalcitrant warts versus those with negative past history (median=28.40 versus 14.92) (p=0.034). Regarding IL22, there was a non-statistically significant association between it and past history of recalcitrant warts among cases group.

Table 6: Association between IL17, IL22 and past history of recalcitrant warts among cases group

	IL17			Test	P
	Mean ± SE.	Median	Min. – Max.		
Past history					
Negative, (n=16)	24.41 ± 5.33	14.92	2.16 – 70.54	U= 374.0	0.034*
Positive, (n=34)	38.05 ± 4.25	28.40	13.89 – 115.11		
	IL22			**Test**	**P**
	Mean ± SE.	**Median**	**Min. – Max.**		
Past history					
Negative,(n=16)	13.05 ± 3.09	8.76	1.67 – 37.15	U= 359.0	0.070
Positive,(n=34)	18.16 ± 1.90	14.47	1.97 – 48.41		

SE: Standard error, Min.: Minimum, Max.: Maximum, U: Mann-Whitney.
P: Comparing the different categories. *: Significant when p<0.05.

Table (7) shows that IL22 and IL17 had a statistically significant positive correlation with each other in cases group as well as in control group (p<0.001 for each).

Table 7: Correlation between IL22 and IL17 among cases and control groups.

	IL22 vs. IL17	
	rs	***p***
Patients	0.973*	<0.001*
Control	0.965*	<0.001*

rs, Spearman used for numerical data.
*: Significant when p<0.05.

Table (8) shows that a receiver operating characteristic curve [9] of IL22 and IL17 was conducted for discrimination between cases and control groups. Moderate accuracy (AUCs) was found for IL22 and IL17 (AUC=0.890, 0.884 respectively). The best cut off values and performance characteristics are shown in table (8).

Table 8: Validity of serum IL22 and IL17 levels for discrimination between cases and control groups.

AUC	95% CI	p	Cut off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
IL22								
0.890	0.825–0.954	<0.001*	≤29.027	84.0	80.0	84.0	80.0	82.22
IL17								
0.884	0.816–0.925	<0.001*	≤43.824	78.0	85.0	86.67	75.56	81.11

"AUC: Area under ROC curve; CI: Confidence interval, PPV, positive predictive value; NPV, negative predictive value. *: P value Significant <0.05."

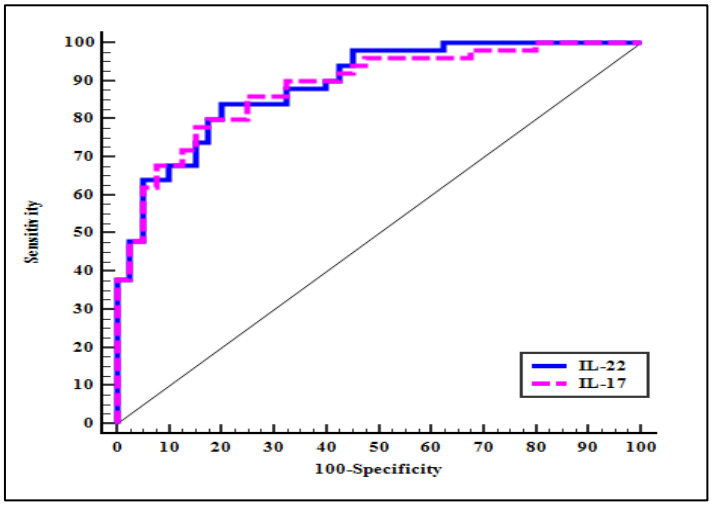

Fig. 3: ROC Curve for serum IL22 and IL17 levels for discrimination between cases and control groups.

Table (9) showed a lower IL22 and IL 17 levels were considered predictors of recalcitrant warts susceptibility in univariable and multivariable analyses

Table 9: Logistic regression analysis for prediction of recalcitrant warts susceptibility.

	Univariate			Multivariate		
	P	**OR**	**95% C.I**	**P**	**OR**	**95% C.I**
Age	0.563	0.986	0.939–1.035			
Gender	0.925	1.041	0.452–2.400			
IL22	<0.001*	0.892	0.853–0.933	0.039*	0.872	0.749–0.916
IL17	<0.001*	0.947	0.927–0.968	0.045*	0.982	0.940–0.990

OR: Odd Ratio; CI, confidence interval. *: Significant <0.05.

DISCUSSION

Our study displayed that the mean age of studied cases was 30.6 ± 8.70, and ranged from 16 to 47 years. They were 27 male (54%) and 23 female (46%)[10]. This was in agreement with a study that reported their patients age ranged from 10 to 62 years. Regarding sex, there was 15 females (60%) and 10 males (40%) who were similar to our results, the wart prevalence was significantly higher in males compared to female cases (2.0% versus 0.9%) (P<0.0001). Likewise, in,[12] study, there were 59 female (42.14%) and 81 male (57.86%)[12]. Overall male to female ratio was 1.37:1.

As regard to disease characteristics, the current study demonstrated that the median disease duration ranged between 1 and 36 months. All cases (100%) had progressive course, and multiple warts. In the same line, Marie et al. [13] found that the mean duration was 7.90 ± 5.11 (1.0 - 18.0) months.

In the current study, affected sites included face in 22 case (44%), arms in 21 case (42%), feet 21 case (42%), hand 16 case (32%), neck 9 cases (18%), fingers 3 cases (6%), toes in 3 cases (6%), others in 4 cases (8%). Also, Marie et al. [13] showed that 9 patients (45%)were presented with common warts; 3 patients (15%) had filiform warts and 1 patient (5%) had periungual wart. Palmoplantar warts (5 cases), plane warts (2 patients), and combined palmoplantar and common warts (4 patients) were recorded in 25%, 10%, and 20% of cases, respectively. 14 patients (70%) had warts in one region, whereas 6 cases (30%) had warts in several regions.

In the present study, recalcitrant wart patients showed a significant reduction in IL-22 level compared to controls (p<0.001). In Contrast to the current results, Marie et al. [13] showed that patients with warts were accompanied by a significant increase in serum values of IL-22 compared with controls. Several immunological cells (such as NK cells, Th-1, Th-17, and Th-22), which are included in HPV clearance, have the ability to release IL-22. In addition, with regard to an infectious setting, IL-22 receptor α expression is improved. INF-α, which is discharged throughout viral dermal infections, raises keratinocyte expression of IL-22 receptor α. Marie et al. [13] displayed that serum values of IL-22 were significantly increased among cases with recurrent warts following preceding management compared to cases with 1st-onset warts.

Furthermore, the IL-22 value was positively correlated with the wart number. An increase in HPV load and resistance to usual therapeutic lines might potently improve antiviral cellular immune responses with the subsequent further discharge of IL-22.

Since every patient in our study was immunologically-competent, the low value of IL-22 may indicate that the immune system is still working to keep a successful TH1 cell-mediated immune response in an effort to manage HPV and reduce its spread. On the other hand, such low IL-22 value wasn't enough to trigger a strong TH1 immune response that could have eliminated HPV infection.In our study, patients with chronic disease had higher values of IL-22 than cases with acute disease; on the other hand, their IL-22 values remained lower than controls. Such an increase in cases of chronic disease may shift the immune response to some extent towards the TH2 profile, with a subsequent increase in viral load and the development of chronic diseases.

In the current study, recalcitrant wart patients showed a statistically significant lower IL17 level in comparison with controls ($p<0.001$). IL17 level showed a statistically significant higher level in patients with positive past history of recalcitrant wart versus those with negative past history (median=38.05 versus 24.41, $p=0.034$). In the same line, the results of [14] study revealed that the cases group displayed a significant reduction in IL-17 values in comparison with controls with a significant -ve relation between IL-17 serum level and both wart duration and number. Mikhael et al. [14] elucidated such decrease in IL-17 by the fact that the main function of IL-17 to keep tissue integrity with subsequent generation of immune response in order to defend against microbes, in particular at epithelial barrier areas this was confirmed also by Stout-Delgado et al[15] study. Particular lifestyle factors were accompanied by a considerable increase in wart development which includes sharing shoes, being near water canals, and having pets within the home [16] which increase the spread of infection between family members. A positive family history of previous contact was recorded in 37 percent of the affected patients[17]. Regarding smoking, Ghanem et al[10] 9 cases (36%) were smokers, while 16 case (64%) were non-smokers which is in agreement with our results.

Our study revealed a positive correlation in contrast to the results of [14] study that displayed a significant -ve relation between IL-17 serum value and both wart duration and number. Such outcomes may be elucidated by the reduction in IL-17A formation with a subsequent increase in viral shedding and significantly compromised Th1 immune responses, as confirmed by Bagri P et al [18] study. These outcomes were in the same line with El-Hamd et al [19] and Ghanem et al [10] researches who demonstrated that serum values of IL-17 were significantly diminished among cases with verruca in comparison with controls. To the best of our knowledge, one immunologic component that may increase the likelihood of HPV infection and recurrence is the decreased blood IL-17 level in wart patients compared to controls.

Our results were also in agreement with Ghanem et al [10] study, a significant reduction in IL-17 level was demonstrated in cases with recalcitrant warts in comparison with the control group (0.49 ng/mL versus 0.77ng/mL in cases with recalcitrant warts and the controls, respectively) ($P<0.001$).

The risk of bacterial infection is higher in IL-17 deficient models due to increased bacterial load, delayed neutrophil recruitment and bacterial clearance. In addition, the possibility of infection by fungi or viruses is elevated in states deficient in IL-17, as in Welch EZ et al [20] study. Cases with leprosy were reported to be associated with significant increases in IL-17 values compared to matched-age and sex-leprosy-free ones. Lepromatous leprosy had the lowest serum values of IL-17. It appears that defective formation of IL-17 plays a main role in leprosy progression, which is mostly reliant on immunity defects, [21] and [22] studies reported a high prevalence of common wart in cases with lupus erythematosus and participate this outcome in the defects in certain immune mechanisms, apart from immunosuppressive therapies.

In our study, IL22 and IL17 showed significant positive correlation with each other in cases as well as in controls ($p<0.001$ for each) . Additionally, IL-17 stimulates the formation of IL-6, which has pro-inflammatory and regulatory actions on the immunity [23]. IL-22 triggers the formation of proinflammatory mediators, which include the S-100A proteins and *CXCL5* [22]. When IL-17 and IL-22 work together, they could trigger the formation of antimicrobial peptides by epithelial cells [24]. Lastly, IL-22 is comprised in epithelial repair [25] and skin protection in chronic infectious diseases. Protection against infections may be reinforced by both the recruitment of inflammatory cells, and enhancement in the functions of the epithelial protective barrier. Additionally, IL-22 and IL-17 encourage the healing process of affected tissue and reinforce epithelial barriers, as a result participating in immunosurveillance[26].

CONCLUSION

Cases with recalcitrant warts were associated with significant increases in serum IL-22 level, and this low value may have a potential function in improving the cell-mediated immune response towards HPV infections. Patients with recalcitrant warts were accompanied by significant reductions in serum IL-17 levels, deficits in IL-17 contributes to the pathophysiology of resistant warts by disrupting the immune system and reducing the number of immune

cells. As a result, IL-17 plays an essential role in the antiviral immune response against HPV infection.

Declarations:
Consent for publication: Not applicable
Availability of data and material: Data are available upon request.
Competing interests: The author(s) declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.
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REFERENCES

1. Al Aboud AM, Nigam PK. Warts are prevalent benign lesions caused by the human papillomavirus (HPV) that occur in the mucosa and skin .National library of medicine 2024; 11:112-35.
2. Simonart T, and de Maertelaer V. Systemic treatments for cutaneous warts: a systematic review J Dermatolog Treat 2012; 23 :72-77.
3. Williamson AL. Recent Developments in Human Papillomavirus (HPV) Vaccinology. Viruses 2023 ; 15:22-30.
4. Joshi S, Anantharaman D, Muwonge R, et al. Evaluation of immune response to single dose of quadrivalent HPV vaccine at 10-year post-vaccination. Vaccine 2023 ;41 :236-45.
5. Macilwraith P, Malsem E, and Dushyanthen S.. The effectiveness of HPV vaccination on the incidence of oropharyngeal cancers in men: a review Infect Agent Cancer2023; 18 :24-30.
6. Bogani G, Ghelardi A, Sopracordevole F, et al. Human papillomavirus (HPV) vaccination: a call for action in Italy. Int J Gynecol Cancer 2023; 33 :1132-9.
7. Abubakar M, Rasool HF, Javed I, et al. Comparative Roles of IL-1, IL-6, IL-10, IL-17, IL-18, 1L-22, IL-33, and IL-37 in Various Cardiovascular Diseases With Potential Insights for Targeted Immunotherapy. Cureus 2023;15: 424-54.
8. Kumaran MS, Bishnoi A, Srivastava N, et al. Significant reduction in the expression of interleukins-17A, 22 and 23A, forkhead box p3 and interferon gamma delineates lichen planus pigmentosus from lichen planus. Arch Dermatol Res 2019; 311 :519-27.
9. de Aguiar Cordeiro R, Reis AT, Lima XTV, et al .Malassezia spp. and Candida spp. from patients with psoriasis exhibit reduced susceptibility to antifungals Clinical Microbiology 2023;54: 169–77.
10. Ghanem AH, Esawy AM, Khalifa NA, Kamal HM. Evaluation of serum interleukin 17 and zinc levels in recalcitrant viral wart. Journal of Cosmetic Dermatology 2020; 19: 954–9.
11. Liu, X., Sun, S., & Liu, D. IL-17D: a less studied cytokine of IL-17 family. International Archives of Allergy and Immunology 2020;181: 618–23.
12. 12.Karki S, Pradhan M, Rai A. Warts among patients visiting the outpatient department of dermatology in a tertiary care centre: a descriptive cross-sectional study. JNMA: Journal of the Nepal Medical Association 2022; 60 :770.
13. Marie REM, Abuzeid AQEM, Attia FM, Anani MM, Gomaa AHA, Atef LM. Serum level of interleukin-22 in patients with cutaneous warts: A case-control study. Journal of Cosmetic Dermatology. 2021; 20: 1782–87.
14. Mikhael NW, El-Fallah AA, Hamed AM. Galectin-3 and Interleukin-17: A potential role in the pathogenesis of human papilloma virus infection Benha Journal of Applied Science 2021;13: 29-3.
15. Stout-Delgado HW, Du W, Shirali AC, Booth CJ, Goldstein DR. Aging promotes neutrophil-induced mortality by augmenting IL-17 production during viral infection. Cell Host & Microbe 2009; 6: 446–56.
16. Kasim K, Amer S, Mosaad M, Abdel-Wahed A, Allam H. Some epidemiologic aspects of common warts in rural primary school children. International Scholarly Research Notices 2013;12:1-6.
17. Essa N, Saleh MA, Mostafa RM, Taha EA, Ismail TA. Prevalence and factors associated with warts in primary school children in Tema District, Sohag Governorate, Egypt. Journal of the Egyptian Public Health Association 2019 ; 94 : 1–6.
18. Bagri P, Anipindi VC, Nguyen PV, et al. Novel role for interleukin-17 in enhancing type 1 helper T cell immunity in the female genital tract following mucosal herpes simplex virus 2 vaccination. Journal of Virology 2017; 91:10–1128.
19. El-Hamd MA, Assaf HA, Nada EA. Possible role of interleukin-17 and macrophage migration inhibitory factor in cutaneous warts. Journal of Cosmetic Dermatology 2018; 17: 1250–53.
20. Welch EZ, Anderson KL, Feldman SR. Interleukin 17 deficiency and implications in cutaneous and systemic diseases. Journal of Dermatology & Dermatologic Surgery 2015; 19: 73–79.
21. Abdallah M, Emam H, Attia E, et al. Estimation of serum level of interleukin-17 and interleukin-4 in leprosy, towards more understanding of leprosy immunopathogenesis. Indian Journal of

Dermatology, Venereology & Leprology 2013;. 79:772-76

22. Korkmaz C, Ürer SM. . Cutaneous warts in patients with lupus erythematosus. Rheumatology International 2004;24: 137–140.
23. Korn T, Bettelli E, Oukka M, et al. IL-17 and Th17 Cells. Annual Review of Immunology. 2009;27: 485–517.
24. Zenewicz LA, Yancopoulos GD, Valenzuela DM, et al . Interleukin-22 but not interleukin-17 provides protection to hepatocytes during acute liver inflammation. Immunity 2007; 27: 647-59.
25. Boniface K, Bernard F-X, Garcia M, et al. IL-22 inhibits epidermal differentiation and induces proinflammatory gene expression and migration of human keratinocytes. The Journal of Immunology 2005;174: 3695–702.
26. Pitta MG, Romano A, Cabantous S, et al . IL-17 and IL-22 are associated with protection against human kala azar caused by Leishmania donovani. The Journal of Clinical Investigation 2009;119: 2379–87.