

## Stress and Coping in Patients with Clinical Manifestations of Human Papillomavirus

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**ABSTRACT** Stressful life events in response to a psychosocial trigger have been reported to negatively affect the course of infections. This study was based on patients with clinical manifestations of human papillomavirus (HPV) infection and a control group of patients with psoriasis who were admitted over a period of one year to the Dermatology Department of Karlovac General Hospital. A total of 122 patients participated in the study, either with a confirmed diagnosis of clinical manifestations of HPV infection (n=66) or in a psoriasis control group (n=56). The aim of this study was to determine which coping strategies are used in patients with clinical manifestations of HPV infection. We used the Recent Life Changes Questionnaire and Brief COPE test for stress evaluation. There were no statically significant differences between adaptive and maladaptive coping strategies comparing patients with HPV and a control group. The difference in specific coping strategies between HPV and control groups showed that self-blame and planning strategies were statistically significantly more common in the HPV group. Patients with HPV with genital warts used maladaptive coping statistically significantly more than patients with non-genital localization of HPV. Patients with HPV who had a higher score of life stress events used maladaptive coping statistically significantly more than patients with a lower life stress events score. The results point to the need for patients with HPV with genital localization and high numbers of stress events to learn how to cope with stress, enabling them to take action and change their ways of coping. There is also a need to integrate psychological intervention into standard care protocols of dermatologic diseases.

**KEY WORDS:** stress, coping, HPV infection

### INTRODUCTION

Stressful life events in response to psychosocial triggers have been reported to negatively affect the course of infections (1). Patients with high stress levels report an increased frequency of human papillomavirus (HPV) infections when compared with people with low stress levels (2). Most people will experience cutaneous warts at some stage of their lives, and if even a small proportion of affected individuals experience psychological distress, this may constitute a significant public health issue (3).

Papillomaviruses are DNA viruses which replicate in the basal layer of skin and mucous tissues. The current classification system, which separates over more than hundred known human papillomaviruses into groups based on similarities in genomic sequences, correlates well with the main clinical categories of HPV infection.

There are several main clinical categories of HPV infection: non-genital cutaneous disease, anogenital diseases, and non-genital mucosal disease.

Within the category of non-genital cutaneous warts, there are several different types. Common warts have a cauliflower-like surface and are typically raised to the surrounding skin surface (3). Genital warts are flesh-colored, soft-to-the-touch bumps that may look like the surface of a cauliflower.

Psychological factors play a significant role in the development and course of a range of diseases, including infectious diseases, such as HPV infection (4).

There is a connection between psychological stressors and dermatoses (e.g. psoriasis, atopic dermatitis, urticaria, warts, herpes simplex, vitiligo, acne, alopecia, prurigo) and different cytokines and mediators produced in the skin. These systems react to stressogenic stimuli and can cause clinical disease in acute or chronic stress. It is significant that stress resistance can be enhanced by personal coping mechanisms, social support, and favorable psychosocial constellations.

There is ample evidence about the bidirectional links between the central nervous system (CNS), immune system, and endocrine system (5,6). The main pathways of stress reactions are the hypothalamic-pituitary-adrenal axis (HPA axis) and the sympathetic, adrenomedullary, and parasympathetic systems (6). Stress may dysregulate the HPA axis and sympathetic nervous system (SAM), leading to higher rates of illness (7-10).

Psychosocial factors influence HPV persistence through moderation of host immune responses (7).

Despite the high prevalence of HPV, most of those infected with HPV will mount a successful immune response and clear the infection. The immune response may differ depending on the duration of the stress and the way of coping.

Stress can increase the severity and duration of infectious diseases and promote reactivation of latent viruses.

A regression of clinical manifestations of HPV has been associated with increased cell-mediated or Th1-type immune responses, and psychological stress has been associated with a decrease in Th1-type immune responses and a shift towards a Th2-type immune response (8-16). These data suggest that psychosocial stress may play a role in HPV infection (17).

On the other hand, there are some studies that do not support significant influence of psychosocial factors. Tiersma *et al.* found no evidence that psychosocial factors influence the course of clinical genital HPV infection and development of abnormal cervical cytology caused by infections of HPV (18). Wilkerson

and Massad found no evidence that stress and depression affect the prevalence of cervical squamous lesions (19,20).

Stress can be controlled by adaptive ways of coping. Coping is not only dealing with the disease on the skin but also coping with the underlining psychological processes. Folkman and Lazarus consider ways of coping to be cognitive and behavioral efforts to deal with external or internal demands that are experienced beyond own resources (21,22).

In situations when stress levels are high enough to disrupt homeostasis, physical or psychosocial symptoms may appear. Some patients use very efficient adaptive coping strategies, but there are many patients with HPV who use maladaptive coping strategies. Maladaptive coping predicts the severity of the disease so it is of utmost importance not only to determine clinical changes of the skin but also to assess the level of stress and ways of coping (23).

Patients can learn to abandon less useful coping strategies and to adopt more efficient coping strategies (24).

If the patients have maladaptive coping mechanisms, we can help them develop more effective coping strategies that would lead to a better overall clinical outcome.

### **Aims of this study:**

To determine which coping strategies are used in patients with clinical manifestations of HPV infection.

Are there differences between clinical manifestations of HPV infection and the control group in ways of coping?

Are there differences between adaptive and maladaptive coping according gender and localization?

Is there a relationship between stress level and different ways of coping in patients with clinical manifestations of HPV infection?

### **PATIENTS AND METHODS**

The study was based on patients with clinical manifestations of HPV infection and control group patients with psoriasis who were admitted over a period of one year to the Dermatology Department of Karlovac General Hospital. We used patients with psoriasis as a control group because of the psychosomatic properties of psoriasis. All included patients gave written consent, and the project was authorized by the ethical committee of Karlovac General Hospital.



Socio-demographic and clinical data were recorded from an electronic database of Karlovac General Hospital.

A total of 122 patients participated in the study, either with a confirmed diagnosis of clinical manifestations of HPV infection ( $n=66$ ) or in a psoriasis control group ( $n=56$ ). There were 56 (45.90%) men and 66 (54.10%) women among the patients. There were 86 (79.49%) married patients and 36 (29.51%) widowed or divorced. Most of them had completed high school, with a mean duration of education 11.6 years, Standard Deviation (SD) 2.951459. The majority of patients lived in urban areas 79 (64.75%), while 43 (35.25%) lived in rural areas.

There were no statistical significant differences between the HPV and a psoriatic control group of patients with regard to variables of sex, age, level of education, marriage status, and living place. Patients with psoriasis were chosen for the control group due to the psychosomatic properties of psoriasis.

The Brief COPE is an abbreviated version of the instrument created based on experiences with patient samples; the factor structure is consistent with the full version of COPE (25-27).

The Brief COPE that was used in this study included 28 questions measuring 14 coping strategies that are presumable adaptive or maladaptive (26).

The test includes six presumable maladaptive strategies (behavioral disengagement, substance use, venting, denial, self-blame, and self-destruction).

There are eight presumable adaptive strategies (seeking emotional support, positive reframing, seeking instrumental support, active coping, planning, humor, acceptance, religion).

Each item is scored from one (I haven't been doing this at all) to four (I've been doing this a lot) on a scale. The possible range of scores for each category was two (not used) to eight (most frequently used). Most frequently used coping strategies scored five to eight; less frequently used strategies scored two to four.

Fourteen coping strategies were classified as adaptive or maladaptive (25-27). The Brief COPE was translated into Croatian and has been previously used in Croatian patients (28). Cronbach's alpha coefficients were used for internal validation of the instruments, and a rate of 0.60 was considered a good internal consistency.

The magnitude of each stressful life event reported by subjects was scored by two independent investigators, blinded to participants' stress and clinical status, using the Recent Life Changes Questionnaire

(RLCQ) (29,30). This validated scale lists 91 different life events that can lead to stress and assigns a numerical value (Life change unit- LCU) ranging from 18 to 123 to the level of stress the event causes.

For the Recent Life Changes Questionnaire, Cronbach's alpha coefficients were used for internal validation of the instruments, and the rate was 0.71.

The Chi-square and t-test were used to analyze the difference in the two proportions. The Mann-Whitney U test was used for analysis of nonparametric data.

Statistical analysis was conducted using SPSS, version 12.

## RESULTS

The result shows that planning, active coping, seeking emotional support, positive reframing, and acceptance are the most frequently used coping mechanisms among patients with HPV. The coping strategies used least are religion and substance use.

Differences in coping strategies between the HPV and control group shows that self-blame and planning strategies are statistically significantly more common in the HPV group (Table 1).

The difference between adaptive and maladaptive coping strategies in patients with HPV was not statistically significant, according to age, duration of clinical changes, duration of therapy, and number of clinical changes.

The difference between genders showed that there was no statistically significant difference in ways of coping.

Patients with HPV with genital warts used maladaptive coping statistically significantly more than patients with non-genital localization of HPV (Table 2).

Patients with HPV who had a higher score of life stress events used maladaptive coping statistically significantly more than patients with a lower life stress events score (Table 3).

## DISCUSSION

There is a limited number of studies demonstrating coping strategies in dermatology patients. Planning, acceptance, and active coping have been reported as the most frequently used coping strategies (31).

There were no statically significant differences between adaptive and maladaptive coping strategies comparing patients with HPV and the psoriasis control group. Our explanation of this fact is that both diseases are prone to stress influence in their clinical manifestations and have the same coping pattern.

**Table 1.** Differences between the human papillomavirus (HPV) and control groups in ways of coping

Way of coping		HPV	Control group	P
		Mean	Mean	
Self-distraction		4.424242	4.964286	0.237506
	Standard Deviation	1.714466	1.815206	
Instrumental support		4.969697	4.785714	0.694114
	Standard Deviation	1,793824	1,832973	
Active coping		5.666667	5.178571	0.283098
	Standard Deviation	1.796988	1.70084	
Denial		3.636364	3.428571	0.649109
	Standard Deviation	1.917325	1.573592	
Substance use		3.090909	2.714286	0.410424
	Standard Deviation	1.974266	1.487158	
Self-blame		4.272727	3.285714	<b>0.035623</b>
	Standard Deviation	1.875379	1.674584	
Humor		4.181818	3.821429	0.407834
	Standard Deviation	1.927669	1.334821	
Planning		5.757576	4.714286	<b>0.03623</b>
	Standard Deviation	2.016034	1.334821	
Emotional support		5.121212	5.285714	0.746471
	Standard Deviation	2.175971	1.696557	
Behavioral disengagement		3.666667	3.678571	0.978407
	Standard Deviation	1.865252	1.492042	
Positive reframing		5.393939	5	0.38865
	Standard Deviation	1.869816	1.632993	
Venting		4.484848	3.892857	0.170807
	Standard Deviation	1.641669	1.685214	
Acceptance		5.666667	5.25	0.276456
	Standard Deviation	1.574537	1.350583	
Religion		3.30303	3.607143	0.502595
	Standard Deviation	1.776317	1.728611	

Warts significantly impair psychosocial wellbeing and quality of life as well as psoriatic lesions (32,33-36).

Coping style has been shown to have a significant influence on patient quality of life and emotional reaction to the disease (37-43).

The results of our study show that denial, planning, acceptance, and active coping are most frequently used among patients with HPV. Problem-focused coping is the most commonly used way of coping. This may be one of the reasons why the disease did not have a more detrimental influence on patient psychological wellbeing (44).

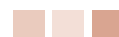
Self-blame and planning are significantly more often used ways of coping in HPV infection, because patients think that their risky behavior caused the illness.

Patients tend to more often use religion for coping and they are less directed towards social network and

support. In our study, religion was the least used way of coping. The reason for this is that religion is more a part of our culture and not of a deep emotional and psychological nature.

Patients with HPV have difficulties such as maladaptive coping, low self-esteem, and feelings of stigma and embarrassment regarding their illness (2).

In our study, patients with HPV who had a higher score of life stress events used maladaptive coping statistically significantly more than patients with a lower life stress events score. On the other hand, there was no statistically significant difference according clinical manifestations. Life stress is a more important predictor of maladaptive coping than mere clinical status of patients. The same results were found in patients with psoriasis who had a higher score of life stress events and used maladaptive coping statistically significantly more than patients with a lower life stress events score.



**Table 2.** Differences between adaptive and maladaptive coping according localization

Location	Way of coping		P
	Adaptive	Maladaptive	
Genital	5	15	<b>0.02847</b>
Non-genital	9	37	

Patients with HPV with genital warts used maladaptive coping statistically significantly more than patients with non-genital localization of HPV. Genital warts significantly impair psychosocial wellbeing (32,33). The psychological impact of anogenital warts should be considered very important (35) and can have more detrimental effects on health than clinical changes.

The psychological aspect of anogenital warts should not be neglected (35). Education of patients with HPV is very important in coping with HPV (32). Psychosocial interventions that should be provided to all patients who are diagnosed with HPV infection can reduce the emotional stress and modulate a patient's coping skills (36).

Stress management decreases life stress and may decrease the odds of cervical neoplasia in women with a history of abnormal Papanicolaou smears (37).

Specific coping strategies and disease perceptions influence health outcome. Patients with higher level of perceived control and greater expression of emotion have better health outcomes over the course of a year than those engaging in passive and avoidant coping behavior (45).

How patients cope with the disease is the key factor in determining outcomes (32). Active coping as an adaptive coping strategy is an action performed to get the best outcome of stress situation. Planning and active coping are the most commonly applied strategies in various skin disease patients. Similar results were found in our study (38).

The results point to the need for skin disease patients, especially with genital localization, to learn how to cope with stress. Patients can be taught to adopt an adaptive way of coping. There is a need for integrating stress management into standard care protocols of dermatologic diseases, especially for patients with HPV with genital localization.

This study had the following limitations: providing retrospective access to patients past history data and explaining the causal sequence among variables. Studies with larger samples are necessary for better understanding of related data.

**Table 3.** Differences between adaptive and maladaptive coping in patients with human papillomavirus (HPV) according to stress level (Life Change Unit score)

Way of coping	Adaptive	Maladaptive	P
Life Change Unit score	282.74	456.71	<b>0.042</b>
Standard Deviation	223.44	253.82	

## CONCLUSION

Patients with HPV with genital warts used maladaptive coping statistically significantly more than patients with non-genital localization of HPV. Patients with HPV who had a higher score of life stress events used maladaptive coping statistically significantly more than patients with a lower life stress events score.

The difference in specific coping strategies between the HPV and control group showed that self-blame and planning strategies were statistically significantly more common in the HPV group.

The results point to the need for HPV patients with genital localization to learn how to cope with stress, enabling them to take action and change their ways of coping.

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