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Level of The Nuclear factor -Erythroid 2–related factor2 in Egyptian patients with cutaneous warts

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Abstract

A wart is a noncancerous growth that may arise in the skin and mucosa. These are benign lesions caused by human papillomavirus (HPV), and over 100 different strains of HPV have been found. Prevalent warts, genital warts, flat warts, deep palmoplantar warts, localised epithelial hyperplasia, epidermodysplasia verruciformis, and plantar cysts are the most common ways that infection manifests. In individuals with genital warts or who are immunocompromised, malignant transformation is often found. While oxidative stress is an intriguing and mostly unexplored option in HPV-mediated carcinogenesis, further investigation is needed. Aim: The goal of this research is to find out whether levels of Nuclear factor-erythroid 2-related factor 2 (Nrf2) are associated to cutaneous warts in Egyptian patients and whether there is a relationship between Nrf2 levels and the severity of the disease. Objectives and Processes: Enzyme-linked immunosorbent assay was used to detect the amounts of Nrf2 in 25 patients with warts and 25 healthy controls (ELISA). Warts are correlated with Nrf2 levels, and these levels were shown to be greater in patients with warts (P =0.001). The most likely conclusion is that higher levels of Nrf2 indicate a role in the development of warts.

Keywords: warts, Nrf2, ELISA.

1.Introduction

Human papillomavirus is a common wart, which occurs in the mucosa and skin (HPV). While common cutaneous warts, genital warts, flat warts, deep palmoplantar warts, localised epithelial hyperplasia, epidermodysplasia verruciformis, and plantar cysts are the predominant symptoms of infection, other conditions may show similar signs and symptoms. In most cases, a malignant change occurs in people with genital warts and individuals with weak immune systems.

While oxidative stress is an intriguing and mostly unexplored option in HPV-mediated carcinogenesis, further investigation is needed. It is well recognised that oxidative stress is able to disturb the cellular redox state, therefore activating redox-sensitive transcription factors. Cell growth and cell death are both positively affected by this signalling cascade.

Redox-sensitive transcription factors such as Nrf2, NF-κB, Activator protein 1, and mitogen-activated protein kinase are also needed to sustain cell viability.

The antioxidant response element (ARE) in the promoter of target genes is recognised by Nrf2, a member of the Cap-N-Collar transcription factor family. a complicated defensive mechanism against xenobiotic and oxidative stress is made possible due to the expression of ARE [4]

Under normal settings, the Nrf2-Keap1 complex is found sequestered in the cytoplasm, where it is targeted for proteasomal degradation. Nrf2 is detached from Keap1 and translocated into the nucleus when cells are subjected to oxidative stress. While the relevance of Nrf2 in skin homeostasis is understood, the exact mechanisms involved are not completely understood.

The highly regulated and sequential expression of a multitude of genes governs the last stages of skin keratinocyte development. When keratinocytes were differentiated, nuclear Nrf2 was translocated to the nucleus, where it acted to promote differentiation-related marker expression, including loricrin and keratin 10.

Therefore, Nrf2 might be involved in the development of warts. The study's goal is to find out whether or not Nrf2 is present in people with warts.

2. Subjects and methods

This case-control research, conducted between June 2020 and December 2020, comprised 25 patients with warts and 25 healthy, matched controls from the dermatology outpatient clinic at Benha University Hospital in Benha, Egypt. Before enrolling, participants provided their informed permission and the project was authorised by the Faculty of Medicine at Benha University's Research Ethics Committee.

2.1. History taking

Patients' demographic data were recorded: name, age, sex and occupation. A detailed history was taken from patients regarding onset, course, duration of warts and recurrence. Also we asked about medical problems including any systemic or skin diseases, drug intake and family history.

2.2 Clinical examination

Full general examination was done to exclude associated systemic diseases and other inflammatory skin diseases, A complete dermatological examination was carried out to determine type, grade and extent of warts and to exclude other chronic dermatological.

2.3. Blood samples

Three mls of venous blood samples were collected from each participant under complete aseptic conditions and put in a serum separating tube and left for 30 minutes till clotting, and then samples were centrifuged at 2000 g for 10 minutes.

The separated serum were aliquoted and stored at (-30°c) till assay.

Determination of level of NRF2 was measured by ELISA Kit following manufacturer manual provided by Shanghai Sunred Biological Technology Company, China, according to the manufacturer's instructions.

2.4 Statistical Analysis

The collected data were tabulated and analyzed using SPSS vs.25. (IBM, Armonk, New York, United states).

3. Results and discussion

3.1 Laboratory results

The current study was carried out on 25 patients with cutaneous warts. The control group included 25 healthy subjects.

Nrf2 had significantly higher levels in all studied wart cases, when compared to control group ($p<0.001$). Table(**1**)

Linear regression analysis was conducted for prediction of warts severity (higher no of warts), using age, gender, BMI, family history and Nrf2 level as confounders. Higher Nrf2 level was suggested to be independent predictor for warts severity Table (**2**).

3.2 Discussion

Warts are non-life-threatening benign lesions seen in the mucosa and skin, caused by the human papillomavirus (HPV), with more than 100 HPV strains known. In most cases, a malignant change occurs in people with genital warts and individuals with weak immune systems.

Nrf2, which has a basic leucine zipper (bZip) domain, controls the production of many antioxidant proteins, including phase II detoxifying enzymes, that protect the cell from the damaging effects of inflammation and injury. It is also capable of supporting cell protection in vitro by induction of antioxidant and detoxifying enzyme and protein production via its binding to the cis-acting ARE. Consider applying:

In our investigation, levels of Nrf2 in all instances of wart were considerably greater than in control groups ($p < 0.001$).

Results of our research show that the number of Nrf2 in cutaneous warts is statistically significantly higher ($p=0.05$) than in controls. The research findings mentioned increased Nrf2 levels as a separate predictor for wart severity.

"A second research found that in the normal or unstressed situation, Nrf2 is degraded by a cluster of proteins that keeps it in the cytoplasm." The normal response to oxidative stress is that Nrf2 is kept in the cytosol. However, when under stress, Nrf2 will move to the nucleus where it attaches to a DNA promoter and triggers the transcription of antioxidative genes and associated proteins [8].

We were able to replicate the findings of previous investigations which showed that Nrf2 levels rise in viruses. One example is findings in HBV and HCMG where Nrf2 is shown to be increased in the serum.

Table (1) Comparison of serum NRF2 concentration between studied and control group.

		Control N=25	**cutaneous warts N=25**	**P**
NRF2 (ng/ml)	**Mean**	0.57	1.93	P3=0.002
	±SD	±0.18	±0.61	

Table (2) Regression analysis for prediction of severity (higher number of lesions).

	Univariable	
	β regression coefficient	p
Age	0.151	0.521
Gender	2.526	0.165
BMI	0.038	0.801
Positive family history	2.696	0.296
Duration	0.175	0.167
cutaneous	1.480	0.290
NRF2	2.553	<0.001

According to previous and ongoing studies, Studies have shown that Hypermethylation of the KEAP1 gene in cervical cancer tissues enhances nuclear expression Nrf2, and decreases cytoplameric expression Keap1, which helps promote tumour growth.

In addition, some investigations concluded that Nrf2 is a contributing factor in the development of psoriasis [11] and vitiligo [12].

Warts have been shown to have higher amounts of Nrf2, making it a suitable target for the illness.

We discovered that there are no published research that assess the amount of Nrf2 in patients with warts.

4. Summary

Our study findings reveal that higher levels of Nrf2 contribute to the development of warts, and provide more information on the function of Nrf2 in cutaneous warts aetiology.

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interests that may conflict Conflicts of interest do not exist.

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