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Evaluation of Granulysin Level in Active Vitiligo

Thesis

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in **Dermatology, Venereology and Andrology**

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Asmaa Harith Mustafa Alkhateeb

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List of Abbreviations

Abb.	Full term
AA	Alopecia areata
AChE	Acetylcholinesterase
AMPs	Antimicrobial peptides
APS	Autoimmune polyglandular syndromes
ATP	Adenosine triphosphate
AUC	Area under the curve
CLM	Confocal laser microscopy
CTLs	Cytotoxic T lymphocytes
DAMP	Damage-associated molecular pattern
DHPR	Dihydropyridine reductase
DOPA	3,4-dioxyphenylalanin
ELISA	Enzyme-Linked Immunosorbent Assay
GNLY	Granulysin
gp100	Glycoprotein 100
H2O2	Hydrogen peroxide
HLA-A2	Human leukocyte antigen
HS	Highly significant
ICAM-1	Intercellular Adhesion Molecule 1
IFN- γ	Interferon-γ
IFN	Interferon-a
IL10	Interleukin10
IL-8	Interleukin 8
IQR	Inter-quartile range
M.tb.	Mycobacterium tuberculosis
MART-1	Melanoma antigen recognized by T cells 1
MCP	Monocyte chemoattractant protein -1
MHC II	Major histocompatibility complex class II
MIP	Macrophage inflammatory protein -1a
MV	Mixed vitiligo
NADH	Nicotinamide adenine dinucleotide
NB-UVB	Narrow-band UVB
NK	Natural killer
NPV	Negative predictive value

List of Abbreviations cont...

Abb.	Full term
NS	Non-significant
NSV	Non-segmental vitiligo
OM, IM	Outer and inner membranes
PAMP	Pathogen-associated molecular pattern
PASI	Psoriasis Area Severity Index
PPV	Positive predictive value
PRI	Potential Repigmentation Index
PRR	Pattern recognition receptor
PsA	Psoriatic arthritis
PUVA	Psoralen and UV-A
RANTES	Regulated upon activation T cell expressed and secreted
RCT	Randomized controlled trial
ROC	Receiver operating characteristic curve
ROS	Reactive oxygen species
S	Significant
SAPLIP	Saposin-like protein
SD	Standard deviation
sIL-2R	Soluble interleukin-2 receptor sIL-2R
SJS	Stevens-Johnson syndrome
SPSS	Statistical Package for Social Science
Σ(sigma)	Summation
SV	Segmental vitiligo
TEN	Toxic epidermal necrolysis
TIM	Topical immunomodulatory
TNF-α	Tumor necrosis factor-α
TREGs	Regulatory T cells
TRP1	Tyrosine-related protein 1
UV	Ultraviolet
VASI	Vitiligo Area Scoring Index
VETF	Vitiligo European Task Force
VETI	Vitiligo Extent Tensity Index
VIDA	Vitiligo disease activity score

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ABSTRACT

Background: Vitiligo is an acquired, a progressive, multifactorial, depigmenting disorder characterized by the appearance of circumscribed white macules in the skin due to chronic, progressive loss of functional melanocytes in the epidermis**.**

Aim of the work: We aimed to evaluate GNLY- levels in stable and active vitiligo patients in comparison to healthy controls.

Patients and Methods: A case-control study which was carried out on 66 subjects: 22 patients with active vitiligo, 22 with stable vitiligo, and 22 age and sex-matched controls. All patients were recruited from the Dermatology Outpatient Clinic of Ain Shams University hospitals during the period from February 2021 to May 2021.

Results: We found a statistically significant difference between vitiligo patients and controls regarding GNLY levels with higher GNLY-levels among cases as compared to control. There were no statistically significant relations between GNLY-levels and gender or age of patients, family history, distribution or duration of vitiligo as well as activity or severity of vitiligo disease. This suggests that GNLY has an important role in vitiligo pathogenesis regardless of the activity, severity, and different disease characteristics. To the best of our knowledge, our study was the first study that measured GNLY-level in vitiligo patients and compare it with controls. Also, compared GNLY level in stable vitiligo versus active vitiligo.

Conclusion: Our findings supported the possible role of GNLY in the pathogenesis of vitiligo. However, measurement of GNLY level can not be used as a discriminating marker between stable and active vitiligo.

Keywords: Granulysin Level, Vitiligo

INTRODUCTION

Vitiligo is an acquired cutaneous disorder of pigmentation of unknown etiology. It is characterized by milky white depigmented macules and patches, often symmetric, whose size increase during the time, relating to the loss of functioning melanocytes. The prevalence ranges from less than 0.1% to more than 2% worldwide, with the disease can appear at any time, and it significantly impairs the patients' quality of life ***(Lotti & D'Erme, 2014)***. Vitiligo susceptibility is not believed to be sex-linked, but 6–38% of patients have family members with the disease indicating a hereditary factor ***(Rezaei et al., 2007).***

The exact etiology of vitiligo is unknown. It is believed that vitiligo is a polygenic trait and that a convergence theory combining elements of different etiological theories across a spectrum of expression is the most accurate etiology***(Garg et al., 2010).***

Research into the pathogenesis of vitiligo suggests that oxidative stress may be the initial event in the destruction of melanocytes. Indeed, melanocytes from patients with vitiligo were found to be more susceptible to oxidative stress than those from unaffected individuals and are more difficult to culture ex-vivo than those from healthy controls ***(Bergqvist & Ezzedine, 2020).***

Many studies have indicated a role for both cellular and humoral immunity in the pathogenesis of vitiligo. Furthermore, Lots of evidence have confirmed that Cytokines that have a crucial function in the development, differentiation, and regulation of immune cells, may play a role in the pathogenesis of vitiligo ***(Singh et al., 2019).***

Granulysin(GNLY) is a cytolytic and proinflammatory peptide that belongs to a family of saposin-like, lipid-binding antimicrobial peptides (AMPs), and co-localizes in the granular compartments of human cytotoxic T lymphocytes (CTLs) and natural killer (NK) cells, along with granzymes and perforin ***(Elgarhy et al., 2015)***.

GNLY expression has been studied in some inflammatory skin diseases, including lichen planus (LP), atopic eczema (AE), and Alopecia areata (AA)***(Pivarcsi et al., 2004; Ono et al., 2014).***

GNLY is a chemoattractant for T lymphocytes, monocytes, and other inflammatory cells. It activates the expression of several cytokines, including, IL-10, IL-1, IL-6, and interferon (IFN)-a ***(Krensky & Clayberger, 2009).***

On the other hand***, Moretti et al. (2002)*** reported a significantly higher expression of pro-inflammatory cytokines with an inhibitory effect on pigmentation, such as IL-6 and TNF-α, in lesional and perilesional skins in vitiligo patients.

To date, no study has addressed the expression of GNLY in vitiligo and assessed its possible role in disease kinetics before. Thus, our study evaluated the expression of GNLY in perilesional skin of vitiligo patients compared with healthy controls to investigate the possible role of GNLY in the pathogenesis of vitiligo.