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ORIGINAL ARTICLE

Evaluation of the Effect of Narrow Band Ultraviolet B versus Methotrexate on Serum Chitotriosidase Level in Psoriasis

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ABSTRACT

Background: Psoriasis is a common, chronic Papulosquamous inflammatory skin disease with an incidence of approximately 2% worldwide. **Aim:** assess serum level of Chitotriosidase **(**CHIIT1) in patients with psoriasis and its relationship with psoriasis area and severity index (PASI) score before and after treatment with narrow-band ultraviolet B (NB-UVB) phototherapy and Methotrexate (MTX). **Materials and methods:** This study was a randomized clinical study included 30 patients with psoriasis vulgaris, ranging in age from 10 to 60 years, who were divided randomly into two groups, group A including 15 patients received NB-UVB treatment and group B received MTX in addition to 15 healthy individuals as a control group, with the same age and sex groups as patients of psoriasis vulgaris. **Results:** The serum level of CHIIT1 shows a statistically significant difference between the three groups; the highest mean CHIIT1 level was in the MTX group (830.2 ± 99.7) compared with both the NB-UVB group (534.2 ± 27.9) and the control group (18.86 ± 2.7). **Conclusion:** CHIIT1 levels in psoriasis are substantially higher than in controls. CHIIT1 level were dramatically reduced during NB-UVB and MTX treatment. CHIIT1 level may serve as a potential biomarker in psoriasis diagnosis and prognosis.

Keyword: Psoriasis, Chitotriosidase, NB-UVB, Methotrexate.

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INTRODUCTION

Psoriasis is characterized by erythematous plaques with sharp boundaries and covered with pearlescent squamae, often with nails or joints affection. The most common form is Plaque psoriasis.1

The cytokines generated by immune cells, T cells, dendritic cells, neutrophils, keratinocytes, and others probably contribute to the development and maintenance of the cutaneous inflammation that is characteristic of psoriasis.2

CHIT1 belongs to chitinase protein family. It is the primary active chitinase in the human body, catalyzing the hydrolysis of substrates that resemble chitin as well as chitin itself. 3

It has been linked to the etiology of numerous human disorders via means of inappropriate tissue remodeling and inflammation induction. 4

In 2020, İlanbey 5 found that Psoriatic individuals have greater serum levels of CHIT1 than healthy controls. Among phototherapy, NB-UVB is most frequently utilized form in the management of psoriasis and numerous skin conditions. 6

MTX is an immunosuppressive medication that reduces the release of pro-inflammatory cytokines such as IL-1β band IL-6, IL-8, TNF-α, and IFN-γ and considered as a gold standard therapy for moderate and severe psoriasis. It has anti-proliferative and anti-inflammatory effects by increasing T cell apoptosis, reducing cell proliferation, alteration cellular adhesion .7

PATIENTS AND METHODS

This study was a randomized clinical study included 30 patients with psoriasis vulgaris, ranging in age from 10 to 60 years, and 15 healthy individuals as a control group, with the same age and sex groups. It was conducted between February 2022 and May 2023 in the Outpatient Clinics of
Dermatology, Venereology and Andrology, Aswan University Hospital, to evaluate the serum level of CHIT1 in psoriatic patients before and after management with NB-UVB phototherapy and MTX.
Exclusion criteria:
The study excluded patients with the following criteria: those who had received NB-UVB phototherapy within the previous three months, those who had hepatic disorders, hematologic diseases, chronic renal failure, infections, or cancer, patients who were managed with systemic or biologic treatment and any systemic treatment modality of psoriasis in the last 3 months, and presence of pregnancy or lactation.

Methods:
Clinical examinations and a complete medical history were performed on all included patients before collecting blood samples:
PASI score measurement:
It is a method for calculating PASI score. Shown below; which includes evaluating erythema (E), induration (I), desquamation (D), and body surface area involvement (A) across four body locations (head [h], trunk [t], upper [u] and lower [l] extremities)8.

The following formula is used to determine the PASI score: The sum of the desquamation, induration, and erythema is multiplied by value of area, then by 0.1 for head, 0.2 for upper limbs, 0.3 for trunk and 0.4 for lower limbs. PASI = 0.1 (Eh + Ih + Dh) Ah + 0.2 (Eu + Iu + Du) Au + 0.3 (Et + It +
Dt) At+ 0.4 (El + Il + Dl) 9.

The severity of the disease was evaluated as:
Mild: if the PASI is below 10.
Moderate: in the range of 10 to 20 PASI
severe: if the PASI exceeds 20.

NB-UVB phototherapy:
For three months, 15 psoriasis vulgaris patients received NB-UVB (311 nm) phototherapy twice a week (on non-consecutive days). Eight narrowband UVB lamps (TL01) of the Waldmann type F 85/100W-01 were installed in the machine. The light spectrum of these lamps ranged from 310 to 315 nm, with a maximum UV-um of 313 nm100L.

The starting dose was 0.25 J/cm², and it was raised by 10%–20% at each session, reaching a maximum of 5 J/cm². The dosage was lowered by 20% or the treatments were temporarily halted when erythema, discomfort, or blistering appeared. Patients were advised to wear "UV goggles" for eye protection when exposed to NB-UVB, and male patients were advised to shield their genitalia.

MTX:
Fifteen patients with psoriasis vulgaris received MTX intramuscularly in dose of (0.3 mg/kg/week) along with folic acid supplementation 5 mg given 24 hours after methotrexate for (10-12 weeks).
Prior to the initial MTX dosage 12 weeks later, LFTs and renal function tests were performed on each patient.

Medical photography: A high-resolution, 18-megapixel Canon EOS 1300D digital camera was used (manufactured in Taiwan), the patients were photographed both at baseline and three months after beginning consistent therapy. Standard lighting and distance were used for the photos.

Assessment of serum level of CHIT1: Methodology of laboratory investigations.
Sample preparation:
Five cc (5 cc) of the patient's blood were drawn from an antecubital vein. Serum separator tubes (SST) were used to collect the sample. The blood sample was centrifuged for 20 minutes at 2000–3000 rpm after being left to clot for Ten to twenty minutes at room temperature. Before being analyzed, the serum was extracted and retained at -30° C. To estimate liver and renal function tests immediately, additional (2 cc) venous blood samples were drawn from the group of MTX patients and placed in plain tubes centrifuged for serum separation.
Determination of serum CHIT1:
Principle of the essay:
The micro-ELISA plate that comes with this kit has already been pre-coated with an antibody that is specific to human CHIT1. The antibody is mixed with samples (or standards) in the micro-ELISA plate.

Calculation of results:
Subtract the average zero standard optical density from the average duplicate readings for each standard and sample. With OD values on the y-axis and standard concentration on the x-axis, plot a four-parameter logistic curve on the log-log axis. You should retest the sample using the proper dilution if its OD exceeds the top limit of the standard curve. The actual concentration is the calculated concentration multiplied by the dilution factor.

Statistical analysis:
The researcher employed SPSS version 24* for data analysis, verification, and coding. Frequencies and percentages were used to represent categorical variables, and the Chi-square test was used to compare the proportions between groups. The mean, median, standard deviation (SD), and range were used to display the quantitative variables.. The correlation between variables was found using Pearson's correlation test. Sensitivity analysis was conducted to detect the diagnostic ability of CHIT1 level for disease prediction. A p-value < 0.05 was considered significant. * IBM_SPSS. Statistical Package for Social Science. Ver.21. Standard version. Copyright © SPSS Inc., 2011-2012. 0

Ethical considerations:
Prior to the study's implementation, the Institutional Review Board (IRB) of Faculty of Medicine - Aswan University granted approval (IRB no.22/1/593). Trial registration was obtained at ClinicalTrials.gov prior to the study (NCT05427175). In addition, A formal consent form was given to every participant.

RESULTS

Table (1): Base line Socio-demographic Differences between the groups studied.

P-value	Control (III) (n=15)	MTX(II) (n=15)	NB-UVB(I) (n=15)	
=0.414*	27.89±3.8	33.55±5.1	31.67±4.5	**Age/year**
	Ivs.III=0.512	IIvs.III=0.236	Ivs.II=0.437	**P-value****
				Sex
=0.509***	6(40%)	7(46.7%)	4(26.7%)	• **Female**
	9(60%)	8(53.3%)	11(73.3%)	• **Male**

Table (2): Effect of Therapeutic Modality on PASI Score.

P-value*	MTX (n=15)	NB-UVB (n=15)	
=0.135	19.35±3.2	13.33±2.2	**PASI before treatment**
=0.401	2.85±0.9	3.91±0.8	**PASI after treatment**
<0.001* **	**<0.001**	**<0.001**	**P-value*****
0.002*	87.21±3.1	66.83±5.3	**%change in PASI Score**

Table (3): Effect of Therapeutic Modality on CHIT1 Level.

P-value*	MTX (n=15)	NB-UVB (n=15)	
=0.014	830.19±99.7	534.19±27.9	**CHIT1 Level before treatment**
=0.030	115.97±30.8	216.19±35.5	**CHIT1 Level after treatment**
<0.001* **	**<0.001**	**<0.001**	**P-value*****
0.021*	81.19±6.3	59.92±6.6	**%changeinCHIT1Level**

Table (4): CHIT1 Level Differences between the studied groups.

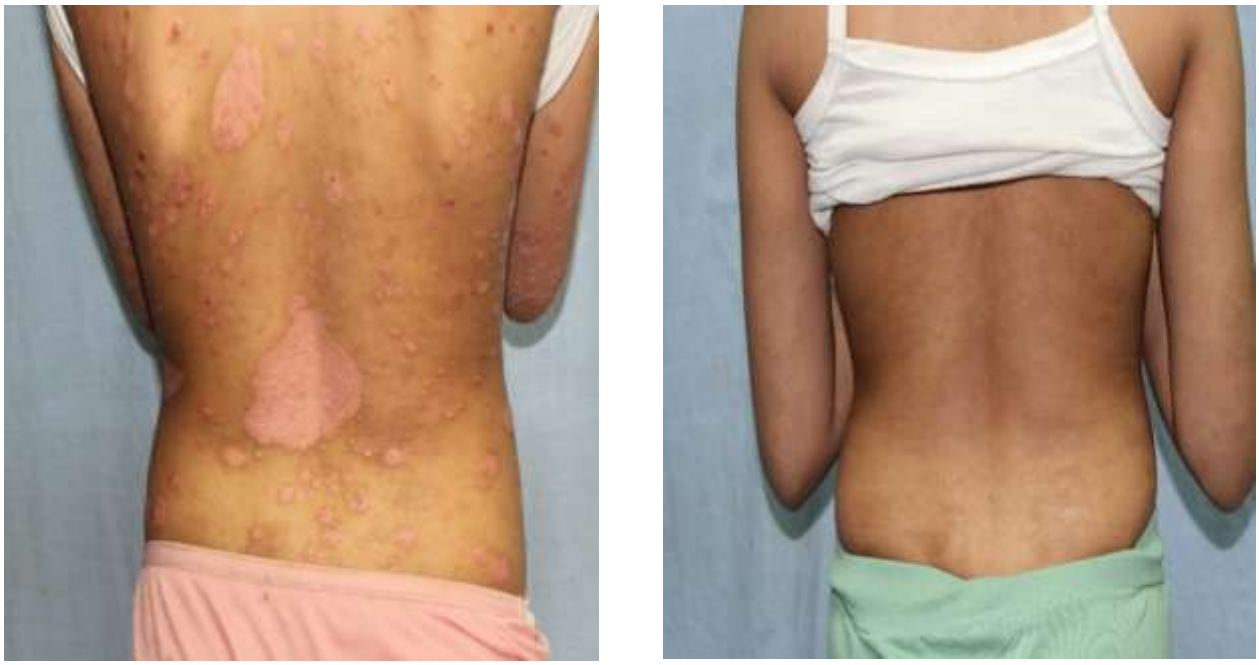
P-value*	Control (III) (n=15)	MTX(II) (n=15)	NB-UVB(I) (n=15)	
			CHIT1Level	
<0.001	18.86±2.7	830.19±99.7	534.19±27.9	• **Mean±SD**
	17(4-42)	683(198-1735)	483(451-781)	• **Median(Range)**
	Ivs.III<0.001	**IIvs.III<0.001**	**Ivs.II=0.006**	**P-value****

Table (5): Correlation between PASI Score% change and CHIT1 Change

PASI% Change(r*(P-value**)	
NB-UVB Group	
0.082(=0.386)	**CHIT1Level%Change**
Methotrexate Group	
0.072(=0.399)	**CHIT1Level%Change**

Table (6): Diagnostic criteria of CHIT1 for Prediction of Disease

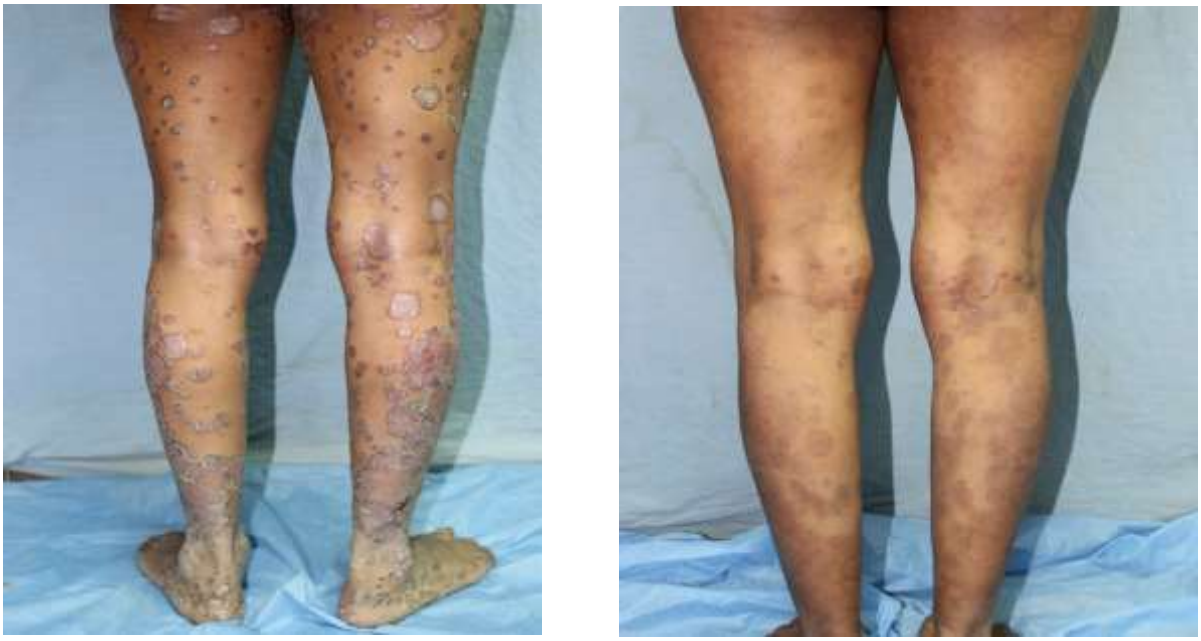
CHIT1Level	Diagnostic criteria
0.967	• **AUC**
0.905-1.000	• **95%CI**
<0.001	• **P-value*** **
95%	• **Accuracy**
97%	• **Sensitivity%**
93%	• **Specificity%**
93%	• **PPV%**
97%	• **NPV%**



A) Before treatment **B) After treatment**

Fig. (1): A 10-year-old child female with plaque psoriasis treated with NB-UVB:

A) before treatment PASI score was 22 and B) after treatment PASI score was 1.



A) Before treatment **B) After treatment**

Fig. (2): male patient, 30-year-old with plaque psoriasis treated with MTX:

A) before treatment PASI score was 41.1 and B) after treatment PASI score was 5.5.

DISCUSSION

psoriasis is a chronic immune-mediated skin and joint condition marked by the invasion of inflammatory cells like T lymphocytes, neutrophils, and macrophages, In addition to keratinocytes' aberrant proliferation and differentiation.10

NB-UVB and MTX are considered widely used effective systemic modalities in the management of chronic plaque psoriasis 11.

Activated macrophages and neutrophils release the CHIT1 enzyme in response to proinflammatory signals. 12,13

In the current study we aimed to assess the possible role of serum CHITI1 in etiopathogenesis and severity of Psoriasis and to study the influence of NB-UVB Versus MTX therapy on the serum CHIT1 level in patients with moderate to severe psoriasis.

In this study, the mean age was 31.67 ± 4.5years in NB UVB group and 33.55 ± 5.1years in MTX group. As regard of sex distribution, there was male predominance between the two psoriatic groups. in the NB-UVB group, about three-quarters 73% was male, and in the MTX group, about one-half 53% (n = 8) was male.

The mean age and sex distribution of the patients and healthy controls did not significantly correlate, according to this study. This finding was in harmony with El-Hamd 14 and Emma15.

In our study, the two groups under study (MTX and NB-UVB) illustrated significant reduction in the mean PASI score after therapy for each group ($p < 0.001$). NB-UVB phototherapy eliminates many pathological changes in lesions of psoriasis, especially the proliferation of keratinocytes. UVB-induced keratinocyte apoptosis can effectively reduce T lymphocytes in the dermis and epidermis, which may be adequate to eradicate psoriatic lesions, in addition, it suppresses the IL-17 and interferon-gamma signaling pathways to reduce psoriatic inflammation. 16,17

Our findings regarding the efficacy of NB-UVB and MTX in management of psoriasis vulgaris agreed with El-Hamd 14 study which conducted on 60 psoriatic patients to evaluate the effects of MTX and NB-UVB phototherapy on serum vitamin D and cathelicidin and levels, as well as to determine their effectiveness in treating psoriasis vulgaris.

Regarding NB-UVB, they found that for three months, NB-UVB phototherapy by itself proved successful improvement of the PASI scores in patients with psoriasis vulgaris.

Our findings also agreed with several previous studies which demonstrated that moderate to severe psoriasis could be effectively treated systemically with NB-UVB phototherapy.18,19

In another study of Johnson20 who uses immunohistochemistry to assess the effect of NB-UVB on Normalized Psoriasis Plaques, it also reported a down modulation of IL-23 and a decrease in INF-γ after NB- UVB treatment. Concerning MTX exerts anti-mitotic and anti-proliferative effects in psoriatic lesions by competitively inhibiting dihydrofolate reductase enzymes, which decreases DNA synthesis. Additionally, it has immuno-modulating and anti-inflammatory properties by inhibiting T-cell activations and causing apoptosis in many immune cells. 14

Moreover, a non-randomized controlled trial study involving 50 patients receiving systemic MTX treatment for moderate to severe psoriasis showed reduction in PASI score from 18 in baseline to 8 after 12 weeks of administration21.

The significant effect of MTX in this study was consistent with number of earlier studies which showed that MTX was a successful systemic treatment for moderate to severe psoriasis. as Kumar22, Van 23 and El-Hamd 14 studies reported Patients with psoriasis vulgaris showed a successful improvement in their PASI scores after three months of MTX therapy alone.

On the opposite side, El-Hamd 14 study did not show significant difference between both groups as the mean PASI percentage change was nearly equal in them (MTX (78.86 ± 10.3) and NB-UVB (78.52 ± 11.4)).

Al-Hamamy24 showed that there was no statistically significant variation in clearance (90% reduction in baseline PASI score) was observed in both MTX and NB-UVB groups (P = 0.674). Due to this discrepancy, further studies are needed to compare both treatments effect on PASI.

Regarding CHIIT1 level in the present study; Statistically significant differences were observed across the three groups. in the mean CHIIT1 level, the highest mean CHIIT1 level was reported in the MTX group (830.2 ± 99.7) compared with both the NB-UVB group (534.2 ± 27.9) and the control group (18.86 ± 2.7).

İlanbey25 who estimated plasma level of CHIT1 by ELISA for 53 Ps patients and 52 healthy controls supporting our findings as Chitotriosidase activity was significantly higher in all the study's patients than in the healthy controls.

The current study revealed that serum CHIIT1 levels were significantly higher in psoriatic patients compared to the controls, the serum level of CHIIT1 was significantly decreased after 24 sessions of NB UVB and 12 weeks of MTX administration as compared with the pre-treatment samples. This reduction was significantly more evident in the MTX group. The mean CHIT1 level percentage change was significantly higher in the MTX (81.2 ± 6.3) than in the NB-UVB (59.9 ± 6.6).
Furthermore, in the present study we found no significant correlation between PASI score and CHIT1 level after treatment by NB UVB, and MTX.

Similarly, İlanbey 25 study revealed no correlation between the PASI scores and CHIT1 activity. By using ROC curve, at a cut-off value of 297 for CHIT1, it had excellent predictive power with high sensitivity 97%, specificity 93%.

Moreover, CHIT1 correctly identified 97% of cases with psoriasis as positive. The test correctly identified 97% of controls as negative. The PPV was 93% and NVP was 97% Overall, the test had 95% accuracy.

Conclusions: NB-UVB or MTX treatment modalities had significant reduction in CHIT1 level with significant better results reported by MTX, so CHIT1 serum level may serve as a potential biomarker for predicting the treatment outcome and prognosis of MTX or NB-UVB in the treatment of psoriasis. as with cut-off value of 297 for CHIT1, it had excellent predictive power with high sensitivity 97%, specificity 93% and accuracy 95%.

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