

Evaluation of Serum Level of Netrin 1 in Psoriatic Arthritis

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Abstract

Psoriasis is resistant interceded persistent and repetitive, fiery dermatosis skin infection. Netrin 1 has a significant part in the pathogenesis of a few immune system sicknesses. This examination is intended to assess the conceivable job of Netrin 1 in the pathogenesis of psoriasis by estimating its level in the serum of psoriatic patients and associate its level with the seriousness, which may help later on treatment of psoriatic injury. This examination included 60 patients experiencing psoriasis vulgaris. Furthermore, 30 obviously solid people of coordinated with age and sex will be picked as a benchmark group. All patients will be exposed to finish history, complete general and dermatological clinical assessment will be finished. Assessment of serum level of netrins 1 in patients and control bunches by ELISA. By contrasting the two gatherings of patients and controls in this investigation there was a huge reduction in the mean serum level of Netrin1 in psoriatic patients contrasted and controls. There was high critical positive connection between's PASI score (seriousness of disease) and level of infection, while there was no huge relationship between's PASI score and illness span or age. There was high huge negative connection between's Netrin1 level and degree likewise there was critical negative relationship between's Netrin1 and Disease span while there was no huge relationship between's Netrin 1 and age and sex. There is a part of Netrin1 in the pathogenesis of psoriasis. Netrin1 can be utilized as marker of sickness degree and illness length.

Keywords: Netrin 1, Psoriatic, Arthritis.

1. Introduction

Psoriasis is a chronic, resistant – interceded foundational illness related with huge bleakness and hindered personal satisfaction. The detailed commonness of psoriasis in nations ranges somewhere in the range of 0.09% and 11.4% making psoriasis a genuine worldwide issue [1].

Psoriasis is a multisystem illness predominately showed as persistent irritation of the skin and described by textured, erythematous patches, papules, and plaques, which are regularly pruritic. Somewhere in the range of 1.3% and 34.7% of people with psoriasis create ongoing, provocative joint inflammation (psoriatic joint pain) that prompts joint disfigurements and incapacity. Somewhere in the range of 4.2% and 69% of all patients experiencing psoriasis create nail changes [2].

People with psoriasis are accounted for to be at expanded danger of creating other genuine clinical conditions, for example, cardiovascular and other non-communicable sicknesses [3].

The etiology of psoriasis stays hazy, in spite of the fact that there is proof for hereditary inclination. The part of the resistant framework in psoriasis causation is likewise a significant subject of examination. In spite of the fact that there is an idea that psoriasis could be an immune system infection, no auto antigen that could be mindful has been characterized at this point. Psoriasis can likewise be incited by outside and inner triggers, including gentle injury, burn from the sun, diseases, fundamental medications and stress [4].

Netrins are a class of proteins engaged with axon direction. They are named after the Sanskrit word "netr", which signifies "one who guides" [5].

Netrin-1 (NTN1) is a protein that in people is encoded by the NTN1 quality. Netrin is remembered for a group of laminin-related discharged proteins. The

capacity of this quality has not yet been characterized, nonetheless, netrin is believed to be associated with axon direction and cell movement during advancement. Changes and loss of articulation of netrin propose that variety in netrin might be engaged with malignancy improvement. Developing lines of confirmations have shown that some direction signs are engaged with guideline of vascular framework elaboration, notwithstanding their part during sensory system improvement. [6].

Vascular endothelial cells play basic obstruction for leukocyte enactment and movement into organs by delivering repellent elements to leukocytes, for example, netrin-1. Movement of incendiary cells to the site of injury is a basic cell reaction to start the evacuation of dead cells and incite a recovery reaction, down regulation of these chemo repellent factors, for example, netrin-1 during organ injury may intensify aggravation [7].

The point of the current investigation was to assess serum levels of netrin 1 protein in patients with psoriasis and its relationship with sickness seriousness.

2. Patients and methods

This case control study, was approved by the local ethic committee of Benha Faculty of Medicine. Informed consent was obtained from each participant before sample collection. The patients' personal data were secured and not published. Patients were not subjected to harmful procedures.

This study was conducted on ninety subjects classified into two groups:

- Patient group: Sixty patients complaining of psoriasis vulgaris.
- Control group: Thirty apparent healthy age and sex matched individual.

Patients had been recruited from Outpatient Clinic of Dermatology, Andrology & Venerology, Benha University Hospitals from Octobre 2019 to January 2020. Clinical assessment was done in Dermatology, Andrology & Venerology Department. Serological assessment was done in Clinical Pathology Department.

2.1 Inclusion criteria

- Patients(male and female) suffered from psoriasis vulgaris.
- Ages were between 16 and 35 years.
- PASI score >12(moderate and severe)
- Patients stopped treatment one month before beginning of the procedure.

Exclusion criteria

- Patient with other autoimmune or allergic diseases.
- Patients with renal or hepatic disease.
- Patient receiving oral immunosuppressive treatment within 6 weeks from sampling
- Patient receiving topical immunosuppressive treatment within 2 weeks from sampling.

All patients were subjected to full history taking, full general examination, Full dermatological examination was done including skin, hair and nail. Psoriasis severity was evaluated by PASI score, All studied subjects were tested for serum level of netrin 1 by enzyme linked immunosorbent assay (ELISA)

2.2 Statistical analysis

The clinical data were recorded on a report form. These data were tabulated and analysed using the computer program SPSS (Statistical package for social science) version 20 to obtain: Descriptive statistics were calculated for the data in the form of: Mean and standard deviation ($\pm SD$). for quantitative data, Frequency and distribution for qualitative data.

2.3 Analytical statistics

In the statistical comparison between the different groups, the significance of difference was tested using one of the following tests; Student's *t*-test:- Used to compare mean of two groups of quantitative data. ANOVA test (F value):-Used to compare mean of more than two groups of quantitative data. A *P* value <0.05 was considered statistically significant.

3. Results

The current study included sixty psoriatic patients; 34 males 56.7% and 26 females 43.3%. Their ages ranges from 18-42 years with a mean age of 38.8±4.97. Thirty clinically free individuals served as a control group ;15 males (50%) and 15 females 50%. Their ages ranged from 20-41 years with a mean age of 42.23±9.91. By comparison between the two groups ,there was no statistically significant difference regarding Age (*p*<0.77) and sex (*p*=0.55) Table (1).

Table (1) Comparison between case and control groups according to gender and age.

| | Case group (60) | | Control group (30) | | Statistical test | P value |
|---------------------|-----------------|------|--------------------|------|-----------------------|---------|
| | No | % | No | % | | |
| Gender | | | | | | |
| Male | 34 | 56.7 | 15 | 50.0 | X ² = 0.36 | 0.55 |
| Female | 26 | 43.3 | 15 | 50.0 | | |
| Age mean ±SD | 38.8 ±4.97 | | 42.23 ±9.91 | | St t= 8.59 | 0.77 |

The mean serum Netrin1 levels were statically significantly lower in psoriatic patients 74.01±34.91 than control group 248.74±360.07 (*p*<0.001), fig (1).

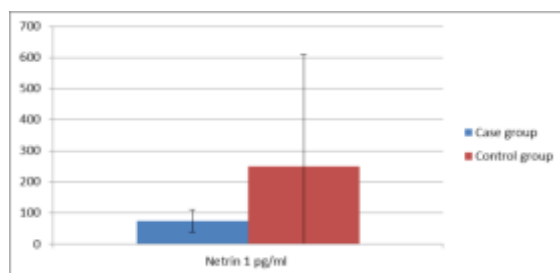


Fig (1) Netrin 1 pg/ml level in patients and control.

Mean serum Netrin 1 levels in females were higher than males with statically significant value (*p*=0.015). Mean serum Netrin 1 level in patients with +ve family history lower than patients with -ve family history with non significant value (*p*=0.22). Table (7) Nertin 1 level of in patients with +ve family history in comparison to -ve family history patients. Mean serum Netrin 1 level in patients with +ve joint manifestation lower than patients

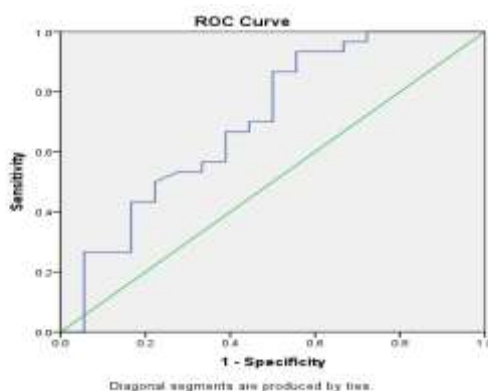
with -ve joint manifestation with non significant value (*p*=0.08). Mean serum Netrin 1 level in patients with +ve recurrence was lower than patients with -ve recurrence with high significant value (*p*=0.001) . Mean serum Netrin 1 level in patients had acute disease was higher than patients had chronic disease with significant value (*p*=0.002) Table (2).

Table (2) Nertin 1 level of male and females.

| Case group (60) | No | Netrin 1 pg/ml Mean \pm SD | Statistical test (t) | P value |
|----------------------------|----|---------------------------------|----------------------|---------|
| Gender | | | | |
| Male | 34 | 64.5 \pm 20.68 | 2.52 | 0.015* |
| Female | 26 | 86.45 \pm 45.03 | | |
| Family history | | | | |
| Present | 6 | 57.17 \pm 27.9 | 1.25 | 0.22 |
| Absent | 54 | 75.88 \pm 35.3 | | |
| Joint manifestation | | | | |
| Present | 12 | 58.42 \pm 23.3 | 1.76 | 0.08 |
| Absent | 48 | 77.91 \pm 36.3 | | |
| Recurrence | | | | |
| Present | 56 | 68.64 \pm 28.14 | 5.43 | <0.001* |
| Absent | 4 | 149.2 \pm 37.07 | | |
| Type | | | | |
| Acute | 6 | 114.5 \pm 60.9 | 3.23 | 0.002* |
| Chronic | 54 | 69.51 \pm 28.28 | | |
| Degree | | | | |
| Moderate | 24 | 108.09 \pm 12.4 | 10.9 | <0.001* |
| Severe | 36 | 51.29 \pm 29.5 | | |

ROC curve analysis showed that a serum level of netrin1 is 88.3 pg/ml. It is decreased in patients with psoriasis. Sensitivity of Netrin 1 was 70%, Specificity

was 56.7%, PPV was 76.4%, NPV was 48.6%, and Accuracy was 65.6%. fig (2).

**Fig (2)** Roc curve.

This study showed that there were high statically significant negative correlation between netrin1 and severity ($p < 0.001$); also there were significant

negative correlation between netrin1 and Disease duration ($p = 0.04$) while there were no significant correlation between netrin 1 and age ($p = 0.21$) Table (3).

Table (3) Correlation between netrin1 and other variables.

| Case group (60) | Netrin 1 pg/ml | |
|------------------|-------------------------|----------|
| | Correlation coefficient | P value |
| Age | 0.164 | 0.21 |
| Disease duration | -0.266 | 0.04* |
| severity | -0.804 | <0.001** |

4. Discussion

In this examination we announced that there was huge contrast between the cases and controls as respect Netrin 1 level lower level of Netrin 1 in cases gathering,

while there is no critical distinction between the contemplated bunches as respect sex and age.

The perplexing communication between the resistant framework and skin cells causes constant aggravation of the skin [8].

The arrangement and upkeep of psoriatic plaques results from an unevenness between calming atoms that advance spilling of leukocyte and multiplication of keratinocytes. The connection between hereditary inclination and fiery action in this illness become more articulated when the powerlessness locus related with enactment or separation of T cell is distinguished [9].

Then again, vascular changes saw in the injuries are believed to be a significant component of the sickness. Truth be told, they are a key part because of the illness, yet in addition it can advance skin aggravation through the expansion of leukocytes. An expanded angiogenesis brought about by psoriatic skin cells and initiation of endothelial cells through supportive of fiery cytokines consequently has a critical connection between the adjusted epidermis and the immunological part of the infection [10].

Favorable to angiogenic factors invigorate endothelial cells, and It initially started to deliver the proteolytic chemicals that separate the extracellular grid, intrusion, relocation and multiplication of endothelial cells there, lastly to the distinctions in another slim cylinder [6].

The impact of netrin-1 on endothelial cell relocation has been appeared in changed investigations. Lu et al. They exhibited the inhibitory impact of netrin-1 on endothelial cell relocation utilizing both the Trans well movement framework and the injury mending model [11].

Treatment of developing vessels with netrin-1, particularly in the end-cell prompts filopodial withdrawal, endothelial cell relocation has been accounted for to incorporate the job of netrin-1 enemy of angiogenic. Nonetheless, different examinations recommend that utilizing comparative models, netrin-1 positively affects endothelial cell movements, and the creators propose that not at all like netrin-1, it will have proangiogenic action [12].

In the current examination there was high huge connection between Netrin 1 and Recurrence and between Netrin 1 and degree, additionally there is huge connection between Netrin 1 and type, and between Netrin 1 and sexual orientation while there is no huge connection between Netrin 1 and family ancestry, joint indications or past treatment.

In an examination by Wu et al. [13] which was directed to it was tracked down that found that therapy with netrin-1 forestalled UV-B radiation-actuated oxidative pressure by decreasing the age of receptive oxygen species (ROS) and articulation of NADPH oxidase 4 (NOX-4). Moreover, therapy with netrin-1 improved UV-B radiation-prompted mitochondrial brokenness by expanding mitochondrial layer potential (MMP) levels and adenosine triphosphate (ATP) creation.

In this examination we tracked down that that there is high critical contrast among moderate and serious degree as respect PASi and Netrin 1 likewise there is huge distinction among moderate and extreme degree as respect age, repeat and past treatment, while there is no

huge contrast among moderate and serious degree as respect Gender, Family history, Joint sign, Type or span.

In our examination we detailed that ROC bend investigation shows that at acut off mark of 88.3 pg/ml Sensitivity of Netrin 1 was 70%, Specificity was 56.7%, PPV was 76.4%, NPV was 48.6%, Accuracy was 65.6%.

Wilson and his associates [14], have performed transitory examines utilizing slope portions of netrin-1, and noticed a maximal movement at 50 ng/ml. In actuality, there was no critical expansion in endothelial cell movement for netrin-1 focus better than 1 ng/ml. Strangely, this is the negligible portion utilized in measures performed by Lu et al. [11] implying that at high dosages netrin-1 could lose its capacity to prompt endothelial cells relocation and even forestalls endothelial cells development.

In this investigation we showed that there was high critical connection between's PASI score and degree, while there is no huge relationship between's PASI score and Disease term or Age.

On the repudiate an examination by Hägg et al. [15], which showed that the lower PASI score in ladies is steady and isn't a consequence of chance varieties. In a multivariable direct relapse, controlling for a few different elements, this distinction remained measurably huge. The distinction altogether yet one of the unmistakable components of the PASI score was additionally huge, both in unadjusted examinations of medians and in the ordinal strategic relapse models changed by age, BMI, infection term, associative PsA, smoking status, and season. Notwithstanding, regarding the head, ladies' and men's PASI scores were equivalent.

Additionally In an unmistakable report from Ireland, it was seen that twice as numerous men (n = 93) got foundational treatment contrasted and ladies (n = 53) [p = 0.015], and that ladies had less extreme psoriasis (experienced by the clinicians) contrasted and men [16].

In a review concentrate from Japan, Sakai et al. [17] investigated the prognostic components for the drawn out result of plaque psoriasis patients (109 men and 60 ladies) in a calculated relapse, and found that men grew more serious psoriasis as per the Dermatology Index of Disease Severity during follow-up contrasted and ladies (p = 0.046), subsequent to adapting to age and BMI.

In our investigation we showed that there was high huge connection between's Netrin1 and degree, additionally there is huge relationship between's Netrin1 and Disease term while there is no huge connection between's Netrin 1 and Age.

5. Conclusion

There is a role of Nerrin1 in the pathogenesis of psoriasis. Netrin1 can be used as indicator of disease degree and disease duration.

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