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Evaluation of Serum Level of Sialic Acid in Patients with Active Vitiligo

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ABSTRACT

Background: Vitiligo is an autoimmune depigmenting disorder of the skin, characterized by well-defined macules and patches due to melanocyte destruction. Sialic acid (SA) possesses antioxidant properties, decreases the activity of anti-melanocyte antibodies and soluble interleukin-2 receptors (SIL-2R), as a result decreasing immune-mediated melanocyte injury. Thus, strengthening its role for unstable vitiligo and encouraging cessation of disease progression

Objectives: This study aimed to evaluate the serum level of sialic acid with the activity of vitiligo.

Patients and methods: This case control study included patients with non-segmental vitiligo (NSV). They were divided into 2 groups: Group A included 30 patients with active vitiligo and group B included 30 patients with stable vitiligo. Control group (C) included 30 age-matched participants. Dermoscopic examination was done by BPLeFoSK criteria for stability in vitiligo and examination of active vitiligo clinically was done by VETI score. Sialic acid was detected by enzyme-linked immunosorbent assay (ELISA).

Results: There was no significant difference between active and stable groups as regards median VETI. There was a significant increase in serum sialic acid among active followed by stable and the least in control group. There was a significant difference between stable and active disease as regards dermoscopic findings. Insignificant relationship was detected between VETI and sialic acid, and age in groups A and B.

Conclusion: In terms of vitiligo cases, serum sialic acid was significantly increased among active, followed by stable, and the least was for control. The studied parameters could act as an essential modality for monitoring vitiligo activity.

Keyword: Sialic acid, Vitiligo, Extent tensity index score, Dermoscopic examination.

INTRODUCTION

Vitiligo is an acquired depigmented skin lesion, characterized by well-defined macules and patches. Vitiligo is a progressive depigmentation disorder resulting from an autoimmune response against melanocytes. It affects about 1.25% of subjects globally, particularly those whose age is 20 years [1, 2].

Vitiligo pathogenesis is complicated and not totally understood. Autoimmune condition, generation of free radicals, impaired adhesion of melanocytes, viral infection, and neurological affection have been considered the most common postulated mechanisms [3]. On the other hand, in recent years, the autoimmune hypothesis has been reported to be the main hypothesis all over the world [4].

There are several forms of vitiligo, which include NSV vitiligo, segmental vitiligo (SV), and mixed vitiligo. In NSV, which is the commonest form of vitiligo, the depigmented patches develop on both sides of the body and often progress slowly. While in SV, the patches are unilateral, in particular in the face and trunk, and don't often cross the opposite side. Mixed vitiligo, in contrast, is an uncommon combined form of SV and NSV [5].

Based on several literatures, it has been demonstrated that melanocyte damage-induced vitiligo may also triggered by the generation of free radicals. To our knowledge, most of the serum proteins are composed of glycoproteins (GPs) where the glycans have terminal SA residues [6]. SAs have a nine-carbon backbone and are a varied family of sugar units. Of note, alteration in protein glycosylation may have an essential function not only in vitiligo pathogenesis, but also in its progression [7].

SA causes its action via irreversible suppression of COX-2, decreasing the generation of free radicals, production of leukotriene C4, a strong melanocyte mitogen, and reduction of leukotriene B4 formation. In addition to the previously mentioned functions, SA also has antioxidant characteristics, decreasing the activity of anti-melanocyte antibodies and SIL-2R, as a result decreasing immune-mediated melanocyte injury.

Furthermore, sialic acid has free radical scavenging characteristics, which could suppress DNA damage, block cellular lipid peroxidation, and antagonize the effects formed by TNF-α. As a result, strengthening its role for unstable vitiligo and promoting a cessation of vitiligo progression, sialic acid helps transform vitiligo from its unstable active form to its stable form [7, 8].

Aim of the study: Evaluation of serum level of sialic acid with the activity of vitiligo.

PATIENTS AND METHODS

This case control study included 60 patients with vitiligo, which were recruited from the Dermatology Department at Mansoura University. The subjects were divided into 2 groups, group A included 30 patients with active vitiligo, group B included 30 patients with stable vitiligo. Group C included 30 participants as a control group. Extension of preexisting lesions and/or the development of new lesions within the last six months are the criteria for active disease [9].

Inclusion criteria: Patients with NSV whose age is more than 18 years and did not receive systemic medications for at least 3 months.

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Exclusion criteria: Pregnant and lactating females, patients on immunosuppressive drugs, patients on chemotherapy, and patients with severe illness.

Methods: All patients were subjected to history taking including personal history (age, sex, residence, occupation, marital status, education level and socioeconomic status), present history (duration of the lesions, previous treatment, and response to treatment), medical history including treatment, phototherapy, oral drugs (corticosteroids and systemic antioxidants) and topical agents (such as corticosteroids), past history of associated diseases [Thyroid disease & diabetes mellitus (DM)], and family history of similar condition. We also asked about the precipitating factors as psychic stress, trauma, sun burn, and photosensitizers (as tolbutamide, sulfonamides, tetracycline, griseofulvin, and phenothiazides).

Complete general and dermatological examination including wood's light were done, percentage of body surface area (BSA) involved was measured by taking the patient's palm as one percent of the total BSA. Dermoscopic examination was done by BPLeFoSK criteria for stability in vitiligo [10] and examination of active vitiligo clinically was done by VETI score [9]. VETI is a system that incorporates 3 components of vitiligo: Extent, stage and progression of disease. The rule of nines is the basis for extent. Stage I is incomplete depigmentation, stage II is complete depigmentation (less than 30% hair whitening), and stage III is complete depigmentation with more than 30% hair whitening. Staging is based on cutaneous and hair pigmentation in vitiligo patches. In VETI, "spreading" is (+1: progressive; 0: stable; −1: regressive).

Technique: Regarding estimation of serum sialic acid, 5 ml of venous blood were taken from all subjects in a sterile test tube. After clot formation, centrifugation of samples at 2000g for ten minutes were done and the sera were separated and stored at -20 °C until analysis. Serum sialic acid was determined by ELISA (quantitative measurement).

Ethical considerations: The study was done after being accepted by The Research Ethics Committee, Mansoura University. All patients provided written informed consents prior to their enrolment. The consent form explicitly outlined their agreement to participate in the study and for the publication of data, ensuring protection of their confidentiality and privacy. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical Analysis

The present data were statistically analysed by SPSS software, version 25 (Inc., PASW statistics for windows, Chicago). Numbers and percentages were used to describe the qualitative data. Following a normality test using the Kolmogorov-Smirnov test, quantitative data were presented using the median for non-normally distributed data and mean ± SD for regularly distributed data. The results were deemed significant at the ≤ 0.05 level. When appropriate, Chi-squared was employed to compare qualitative data between groups. The parametric variables between at least three groups were assessed using the One Way ANOVA test. The non-parametric variable between two groups was evaluated using the Mann Whitney Test (Z test).

RESULTS

Table **(1)** displayed that there was insignificant difference between the studied groups as regards mean age, sex distribution and family history. There was no significant difference between active and stable groups as regards median vitiligo extent tensity index score (VETI). There was a significant higher median serum sialic acid among active followed by stable and the least was for control group (P<0.001).

Table (1): Demographic characteristics, VETI, Sialic acid of studied vitiligo patients

	Active (n=30)	Stable (n=30)	Control (n=30)	Test of significance
Age (Years)	39.3 ± 14.0)	39.5 ± 13.0)	40.6 ± 13.0)	F=0.07 P=0.9
Gender n (%) Male Female	 12 (40) 18 (60)	 9 (30) 21 (70)	 14 (46.7) 16 (53.3)	χ^2=1.7 P=0.4
Occupation n (%) Housewife Employee Driver Nurse Farmer Student	 3 (10) 5 (16.7) 4 (13.3) 4 (13.3) 7 (23.3) 7 (23.3)	 3 (10) 17 (56.7) 3 (10) 5 (16.7) 1 (3.3) 1 (3.3)	 0 (0) 17 (56.7) 0 (0) 0 (0) 13 (43.3) 0 (0)	 χ^2=39.8 P<0.001
Family history Negative Positive	 21 (70) 9 (30)	 21 (70) 9 (30)	 30 (100) 0 (0)	 ---
VETI Median (min-max) IQR	 0.73 (0.05-7.6) 1.08	 0.71 (0.06-74.12) 1.9	 	 **Z=0.26** **P=0.7**
Sialic acid Median (min-max) IQR	 0.70 (0.02-2.3) 0.9	 0.25 (0.04-0.96) 1.9	 0 .09 (0-0.85) 0.09	 χ2=38.6 P<0.001*

VETI: Vitiligo Extent and Therapy Index, **F**: F-statistic (used in One-Way ANOVA Test), **P**: Probability value (p-value), **χ²**: Chi-Square Test, **Z**: Mann-Whitney U Test, **n**: Number of participants, **%**: Percentage, **SD**: Standard Deviation, **IQR**: Interquartile Range, **Min-max**: Minimum-maximum range.

Table **(2)** displayed that there was a significant difference between stable and active disease as regards dermoscopic findings (**P<0.001).**

Table (2): Dermoscopic findings among studied groups

	Active (n=30)	Stable (n=30)	Test of significance
Median	**-1.00**	**2**	**Z=6.9**
Min-max	**-4.0- 1.0**	**2-3**	
IQR	**2**	**0**	

Z: Mann-Whitney U Test, **n**: Number of participants, **Min-max**: Minimum-maximum range, **IQR**: Interquartile Range.

Table **(3)** showed that there was a significant negative relationship between VETI score and dermoscopic findings (r=-0.48) among active group and statistically significant positive correlation between VETI & dermoscopic findings among stable group (r=0.7). No significant correlation was detected between VETI and serum sialic acid, age in both groups (p > 0.05).

Table (3): Relationship between VETI, sr sialic acid and dermoscope among studied groups

	Active gp (n=30)	Stable gp (n=30)
	VETI	
Dermoscope r p	 -0.48 0.006	 0.7 <0.001
Sr sialic acid r p	 -0,27 0.1	 -0.1 0.4
Age r p	 -0.1 0.3	 0.3 0.06

VETI: Vitiligo Extent and Therapy Index, **Sr**: Serum, **r**: Pearson or Spearman correlation coefficient, **p**: Probability value (p-value), **gp**: Group, **n**: Number of participants.

DISCUSSION

Vitiligo is a common depigmented skin disorder characterized by melanocyte destruction**.** Generation of free radicals has been reported to have main role in melanocyte destruction. SA is accompanied by oxidative protein damage [7]**.** The majority of ligands for the selectin family of cell adhesion molecules require SAs in order to mediate leukocyte rolling along the endothelium and other immune cell-to-immune cell interactions [11]. Alterations in protein glycosylation has an essential role not only in disease pathogenesis, but also in its progression [7]**.** It has been demonstrated that generation of free radicals and tissue damage are linked to changes in glycoprotein (GP expression). Examining the profile of SA values will give the first indication of disease activity since they represent glycosylation alterations and acute-phase reactions in disorders [7, 12].

Dermoscopy could be utilized as a non-invasive modality in terms of vitiligo assessment and diagnosis. In addition, it could have an essential role in the determination of vitiligo activity [13, 14].

This case-control study was conducted on 60 Egyptian cases with vitiligo recruited from Mansoura University Hospital Outpatient Clinics, Mansoura, Egypt. The studied subjects were divided into 3 groups: 30 healthy subjects in the control group, 30 active vitiligo patients' group, and 30 stable vitiligo patients' group. Our study was conducted on 14 males and 16 females in the control group and 35 males and 55 females in the vitiligo group. There was no statistically significant difference in the mean age of patients in the vitiligo group (30-51 years) in comparison with normal control ones (31.5-52.3 years). In agreement with our study, **Kaur *et al.*** [15] conducted their study on a total of 50 cases with vitiligo who were divided into two groups: 25 cases with active vitiligo and 25 with stable vitiligo (mean age was 33.6 ± 15.7 years). Male to female (M/F) ratio was 54/46. Basal hypopigmentation was recorded in all cases, but with various degrees of affection.

Our study illustrated that the mean age was 40 years, which is in accordance with **Mohr *et al.*** [16] who revealed that the mean age in their studied vitiligo cases was 43. In contrast, a Korean research study recorded higher incidences at ages five to fifteen years (16.05%) and 45 to 55 years (16.5%) [17]. Whereas, another research study in Taiwan recorded the age of onset as being from 40 to 59 years old [18].

In our study, male to female ratio among vitiligo group was 35/55 which is in agreement with **Mohr *et al.*** [17] who revealed that vitiligo was reported in 1843 (68.5%) women versus 846 (31.5%) in male.

The current study revealed that there was no significant difference in occupation between the studied groups. On the other hand, **Abdallah *et al.*** [19] reported that most of their studied vitiligo cases were employee (34.9%), followed by non-working cases (34.9%) and lastly farmers (9.3%).

The present study revealed that there was insignificant difference in mean family history between the studied groups. Mean negative family history of active (21) stable (21) control (30), in comparison with mean positive family history. active (9), stable (9), control (0). This is in accordance with **Abdallah and his colleagues** [19] who revealed that family history of studied group of comparable state was positive in ten cases (11.6%).

With regard to the associated dermatologic disorders, our study displayed that the majority of the studied cases had no associated dermatologic disorders (80%), while atopic eczema and psoriasis were recorded in 2.3% and 4.7% of the studied cases respectively. With regard to the associated systemic disorders, the present study displayed that 72.1% of the studied cases had no associated systemic disorders, while DM, thyroid disease, hypertension and hepatitis were recorded in 9.3%, 4.7%, 9.3%, and 4.7% of the studied cases respectively**.** This is almost in line with an assessment conducted in China on 815 subjects, which found that 15.7% of them had family history [20]. According to a study done in Saudi Arabia on 111 vitiligo patients, consanguinity was found in 32.4% of cases and consanguinity between first-degree cousins was recorded in 22.5%, suggesting that vitiligo may be an inherited condition. The onset age was earlier in consanguineous cases [21].

Our study found that there was a significant increase in serum sialic acid among active followed by stable and the least was for control group (0.7, 0.25 & 0.09, respectively) (**P<0.001)**. Likewise, **Banerjee *et al.*** [7] have displayed that active vitiligo cases were accompanied by a significant increase in SA value compared to the controls (P < 0.0001).

Our study revealed that there was significant increase median serum sialic acid among active followed by stable and the least was for control group (0.7, 0.25 & 0.09 respectively) (**P<0.001***). Likewise, **Ines *et al.*** [22] revealed that the active vitiligo cases were associated with a significant elevation in serum MDA values compared to stable ones.

Our study illustrated that there was a positive significant relationship between dermoscopic findings and VETI score in stable group (r=0.7, p<0.001). There was moderate negative relationship between VETI score and dermoscopic findings (r=-0.48, p<0.05) among active group. There was insignificant relationship between VETI and serum SA among both active and stable groups. There was no relationship between age and VETI score in stable group (r=0.3, p=0.06). There was negative relationship between VETI score and age among active group (r=-0.1, p=0.3). There was negative relationship between duration and VETI score in stable group (r=-0.2, p=0.1). There was no relationship between VETI score and duration (r=0.1, p=0.5) among active group. There was negative relationship between serum sialic acid and dermoscopic findings among both active group (r=-0.1, p =0.59).

There was a weak negative relationship between serum SA and dermoscopic findings among active and stable groups (p =0.54). There was insignificant difference in serum sialic acid and gender (P=0.6). There was insignificant difference in VETI score and gender (P=0.5).

CONCLUSION

In conclusion in terms of vitiligo cases, serum sialic acid was significantly increased among active, followed by stable, and the least was for control. The parameters studied could act as an essential modality for monitoring vitiligo activity.

- **Conflict of interest:** None.
- **Fund:** None.
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REFERENCES

1. **Mumtaz H, Anis S, Akhtar A *et al.* (2020)**: Efficacy of Tacrolimus Versus Clobetasol in the Treatment of Vitiligo. Cureus, 12: e11985.
2. **Abdelmoneim TA, Aljarbou AN, Alfarouk KO *et al.* (2018)**: The prevalence of vitiligo variants in association with helicobacter pylori infection. American Journal of Dermatology and Venereology, 7: 1-5.
3. **Benincasa G, Di Spigna G, Cappelli C *et al.* (2019)**: High incidence of MTHFR, CBS, and MTRR polymorphisms in vitiligo patients. Preliminary report in a retrospective study. Eur Rev Med Pharmacol Sci., 23: 471-8.
4. **Iannella G, Greco A, Didona D *et al.* (2016)**: Vitiligo: Pathogenesis, clinical variants and treatment approaches. Autoimmun Rev., 15: 335-43.
5. **Dellatorre G, Silva de Castro CC (2020)**: Noncultured epidermal cell suspension for the treatment of recalcitrant segmental vitiligo in a solid-organ transplant recipient. An Bras Dermatol., 95: 257-8.
6. **Xie Y, Sheng Y, Li Q *et al.* (2020)**: Determination of the glycoprotein specificity of lectins on cell membranes through oxidative proteomics. Chem Sci., 11: 9501-12.
7. **Banerjee N, Gayen S, Modak D *et al.* (2019)**: Systemic Redox Imbalance Along with Increased Serum Sialic Acid is Prevalent in Patients with Active Vitiligo: A Study from a Tertiary Care Teaching Hospital of Eastern India. Indian J Dermatol., 64: 97-100.
8. **Grover C, Desai P (2020)**: Vitiligo Onset in Late Age. Comprehensive Textbook on Vitiligo, 4:34-94.
9. **Taïeb A, Picardo M, memberso V (2007)**: The definition and assessment of vitiligo: a consensus report of the Vitiligo European Task Force. Pigment cell research, 20: 27-35.
10. **Ashwini P, Sushmitha D, Veeranna S (2020)**: Vitiligo with special emphasis on vitiligo surgery. Archives of Medicine and Health Sciences, 8: 140-6.
11. **Varki A (2008)**: Sialic acids in human health and disease. Trends in molecular medicine. 14: 351-60.
12. **Rizwan S, ReddySekhar P, MalikAsrar B (2014)**: Reactive oxygen species in inflammation and tissue injury. Antioxidants & redox signaling, 20 (7): 1126-67.
13. **Ibrahim S, Hegazy R, Gawdat H *et al.* (2022)**: Differentiating active from stable vitiligo: the role of dermoscopic findings and their relation to CXCL10. Journal of Cosmetic Dermatology, 21: 4651-8.
14. **Jha AK, Sonthalia S, Lallas A (2018)**: Dermoscopy as an evolving tool to assess vitiligo activity. Journal of the American Academy of Dermatology. 78: 1017-9.
15. **Kaur G, Punia R, Kundu R *et al.* (2020)**: Evaluation of active and stable stages of vitiligo using S-100 and human melanoma black-45 immunostains. Indian Journal of Dermatopathology and Diagnostic Dermatology, 7: 2-6.
16. **Lee H, Lee M, Lee D *et al.* (2015)**: Prevalence of vitiligo and associated comorbidities in Korea. Yonsei medical journal, 56: 719.
17. **Mohr N, Petersen J, Kirsten N *et al.* (2021)**: Epidemiology of vitiligo–a dual population-based approach. Clinical Epidemiology, 13: 373-382.
18. **Chen Y, Chen Y, Hwang C *et al.* (2015)**: Comorbidity profiles in association with vitiligo: a nationwide population-based study in Taiwan. Journal of the European Academy of Dermatology and Venereology, 29: 1362-9.
19. **Abdallah I, Hussein O, Abdelmagid A (2020)**: Epidemiological study of vitiligo in damanhour teaching hospital. Benha Medical Journal, 37: 297-304.
20. **Sun X, Xu A, Wei X *et al.* (2006)**: Genetic epidemiology of vitiligo: a study of 815 probands and their families from south China. International journal of dermatology, 45: 1176-81.
21. **Alzolibani A (2009)**: Genetic epidemiology and heritability of vitiligo in the Qassim region of Saudi Arabia. Acta Dermatovenerol Alp Panonica Adriat., 18: 119-25.
22. **Ines D, Sonia B, Riadh B *et al.* (2006)**: A comparative study of oxidant–antioxidant status in stable and active vitiligo patients. Archives of dermatological research, 298: 147-52.