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Comparative Analysis of the Most Used Versus the Recently Developed Vitiligo Activity and Extent Scores and Their Change with Treatment

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ABSTRACT

Introduction: There are diverse assessment tools for vitiligo, with no standardized approach that helps unify treatment outcome measures. Thus, comparing different treatment modalities and developing evidence-based recommendations for vitiligo management has been quite challenging.

Objectives: We compared the most commonly used tools assessing both vitiligo activity and extent, namely, Vitiligo Disease Activity Score (VIDA) and Vitiligo Area and Severity Index (VASI) score to their newly developed counterparts, namely, Vitiligo Extent Score Plus (VES plus) and Vitiligo Signs of Activity score (VSAS), to provide insights that would help set recommendations for a unified outcome assessment protocol for vitiligo patients.

Methods: Thirty-six active non-segmental vitiligo cases were recruited, 30 of whom completed 48 sessions of narrow band ultraviolet B (NB-UVB). Patients were assessed for both extent and activity both before and after treatment with NB-UVB. Scores were correlated. Additionally, VES plus was assessed for its reliability in comparison to VASI score.

Results: Both extent (VASI and VES plus) and activity scores (VIDA and VSAS) showed significant improvement following treatment. Additionally, VES plus and VASI were positively correlating both before and after treatment as well as their percent change. Furthermore, VES plus proved as reliable as VASI. Regarding activity scores, total, hypochromic and Koebner VSAS only correlated with VIDA following treatment. Confetti VSAS neither correlated with VIDA before nor after treatment.

Conclusions: VES plus and VASI scores have proven of comparable reliability. While examination-based VSAS score comes as an additive tool to the history-based VIDA score.

Introduction

Vitiligo is a chronic depigmenting skin disorder that can be cosmetically disfiguring with high psychological burden [1]. Treatment is quite challenging [2] with no standardized assessment tools for its evaluation and follow-up of treatment response as well as for comparing different treatment modalities. This, in turn, hinders comparison of different clinical trials and the development of evidence-based recommendations [3-7].

Various tools are currently available for assessing vitiligo extent and response to treatment. Since re-pigmentation is the most important reported treatment outcome [4], limitation to the previously developed Vitiligo Extent Score (VES score) was disregarding pigmentation [7]. Thus, Vitiligo Extent Score Plus (VES plus score) was developed that considered both extent and follicular pigmentation [8]. Accordingly, VES plus score stands as an alternative tool to Vitiligo Area and Severity Index (VASI), which is the most cited and used vitiligo extent assessment tool [9,10]. Both VES plus and VASI scores consider extent as well as follicular pigmentation. However, VASI score, despite being widely used [3], is more time-consuming [9,10] since it is manually calculated [9], in comparison to VES plus score, which is calculated online [7]. Additionally, VES plus has been pointed out to detect small changes in the extent of vitiligo, which adds to its privilege [11,12].

Regarding vitiligo activity, history-based Vitiligo Disease Activity Score (VIDA) has been the most used tool [13]. It was only in 2020, when examination-based Vitiligo Signs Activity Score (VSAS) was introduced taking into account different signs of vitiligo activity [14].

Objectives

The aim of this work is to provide some insights in the most recently introduced vitiligo extent score; namely, VES plus [8] in comparison to the most used one; namely, VASI score [9]. Additionally, we aimed at evaluating examination based VSAS, which is the first vitiligo assessment tool that considers solely clinical signs of vitiligo activity [14] in comparison to the most used and validated tool; VIDA score [13]. This study provides a cohort of vitiligo patients to evaluate change in the aforementioned extent and activity scores to allow for a deeper understanding and interpretability of change in these scores and their utility in follow up of vitiligo patients.

Methods

The study was conducted at the Vitiligo Clinic, Cairo University Hospitals. Thirty-six active Non segmental vitiligo (NSV) patients aging ≥ 18 years old were recruited. A VIDA score ≥2 was set as an inclusion criterion to ensure recent vitiligo activity and monitor its change following treatment. Of the 36 patients, only 30 patients completed the study.

Thorough history was taken for different vitiligo characteristics including duration and age of onset. Baseline assessments for vitiligo activity and extent as well as pigmentation were carried out. Vitiligo activity was evaluated using total VSAS, Koebner VSAS, confetti VSAS and hypochromic VSAS [14], together with the history-based VIDA score [13]. Vitiligo extent and pigmentation were evaluated using both VES plus [8] and VASI scores [9].

Both VSAS and VES plus, available through online vitiligo calculator https://www.vitiligo-calculator.com, depend upon diagrammatic representation of different body sites. In VES plus, diagrams representing different extents of vitiligo with option of adding extent of follicular pigmentation within each site are available. Final VES plus score is developed by automatically summing the extent in different affected sites after deducting extent of follicular pigmentation [8]. In VSAS, the three main signs of vitiligo activity; koebnerization type IIB, confetti-like depigmentation and hypochromic/ ill-defined edges, are recorded for different body sites giving a total activity score out of 15, for all signs as total VSAS, where one or more signs of activity within one site scores 1 out of 15, and for each sign separately as Koebner, hypochromic and confetti VSAS [14].

Regarding VIDA score, it is mainly based on the duration since the date of last activity, which is essentially given by history, in the form of expansion of old lesions, koebnerization or development of new lesions [13]. As for VASI, extent of vitiligo as per hand units is multiplied by extent of depigmentation in different body sites, which are added together to get total VASI score [9].

Total body narrow band ultraviolet B (NBUVB) was chosen as a unified treatment protocol that achieves both re-pigmentation and stabilization [15]; thus, offering change in both extent and activity scores. Sessions were delivered by a UV 100 L; Waldmann GmbH cabinet with 40 narrow band UVB fluorescent tubes (Philips TL 01, 100 W, Philips company), an emission spectrum of 310-315 nm was used. Patients received 3 sessions per week on non-consecutive days for a total of 48 sessions.

Following 48 sessions of NB-UVB, patients were reassessed for both activity using VIDA and VSAS scores and extent using VES plus and VASI scores.

Statistical Methods

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp.). Data was summarized using mean, standard deviation, median, minimum, and maximum in quantitative data and using

frequency (count) and relative frequency (percentage) for categorical data. For comparison of serial measurements within each patient, the non-parametric Wilcoxon signed rank test was used. Correlations between quantitative variables were done using Spearman correlation coefficient. Testing for across items reliability (internal consistency) was done using the Intra Class Coefficient (ICC) and Cronbach's alpha reliability coefficient with their 95% confidence interval (95%CI). P values less than 0.05 were considered as statistically significant.

Results

Thirty-six patients were recruited, of whom 30 patients completed the 48 sessions of NB-UVB. Of those who completed the NB-UVB sessions, nine were males and twenty-one were females. Patients had mean age of 29.6 ± 13.7 and an average disease duration of 92.17 ± 83.08 months. The demographic data of the patients are summarized in Table 1

Baseline assessment for vitiligo extent revealed a VES plus score area of 3.39 ± 3.66 and a VASI score of 4.38 ± 4.11. Regarding vitiligo activity, twenty-four patients (80%) had a VIDA score of +4 and mean VIDA score was 3.77±0.5. Regarding VSAS score, patients had a mean total VSAS, confetti VSAS, Koebner VSAS and hypochromic VSAS of 6.63 ± 2.9, 1.47 ± 1.46, 1.67 ± 1.77 and 6.1 ± 3.03 respectively.

After completing 48 sessions of NB-UVB, significant improvement was evident in both activity and extent scores (P = 0.01). Patients had a mean VES plus score of 1.86 ± 2.15 and a mean VASI score of 2.81 ± 2.58; while mean VIDA score was 2.5 ± 0.82 and mean total VSAS, Koebner VSAS, hypochromic VSAS and confetti-VSAS were 0.83 ± 1.34, 0.23 ± 0.57, 0.63 ± 1.22 and 0.13 ± 0.35 respectively. The clinical data of the patients are summarized in Table 1.

On correlating both extent scores, namely, VES plus and VASI, they were strongly positively correlating both before and after NB-UVB as well as their percent change (r = 0.936, 0.97 and 0.723, respectively, P < 0.001) (Figure 1).

Table 1. Clinical and Demographic Data of the Patients Who Completed the Study (N = 30).

Characteristics			
Sex (%)	Females	21 (70%)	
	Males	9 (30%)	
Age (years)	Mean ± SD (Range)	29.6 ± 13.7 (18–61)	
Age of onset (years)	Mean ± SD (Range)	22 ±13.01 (6–56)	
Duration of disease (months)	Mean ± SD (Range)	92.17 ± 83.08 (3–360)	
Skin phototype (%)	III	14 (46.7%)	
	IV	16 (53.3%)	
Associated with stress or trauma (%)		24 (80%)	
Family history of vitiligo (%)		10 (33.3%)	
Family history of autoimmune disease (%)		4 (13.30%)	
Clinical assessment scores			
Cases	Before NB-UVB	After NB-UVB	P-value
	Mean ± SD (Range)	Mean ± SD (Range)	
VIDA score	3.77±0.5 (2-4)	2.5 ± 0.82 (2–4)	< 0.001
VIDA score (%)			
2	1(3.33%)	20(66.66%)	
3	5(16.66%)	3(10%)	
4	24(80%)	6(20%)	
VASI score	4.38 ± 4.11(0.33–15.85)	2.81 ± 2.58 (0.17–10.62)	< 0.001
VES plus score	3.39 ± 3.66 (0.33 –13.33)	1.86 ± 2.15 (0.07–9.31)	< 0.001
Total VSAS score	6.63 ± 2.9 (2–14)	0.83 ± 1.34 (0–5)	< 0.001
Confetti VSAS score	1.47 ± 1.46 (0–6)	0.13 ± 0.35 (0–1)	< 0.001
Koebner VSAS score	1.67 ± 1.77 (0–6)	0.23 ± 0.57 (0–2)	< 0.001
Hypochromic VSAS	6.1±3.03 (2-14)	0.63±1.22 (0-5)	< 0.001

NB-UVB = narrow band ultraviolet B; SD = standard deviation; VIDA = Vitiligo Disease Activity Score; VES = Vitiligo Extent Score; VSAS = Vitiligo Signs of Activity score.

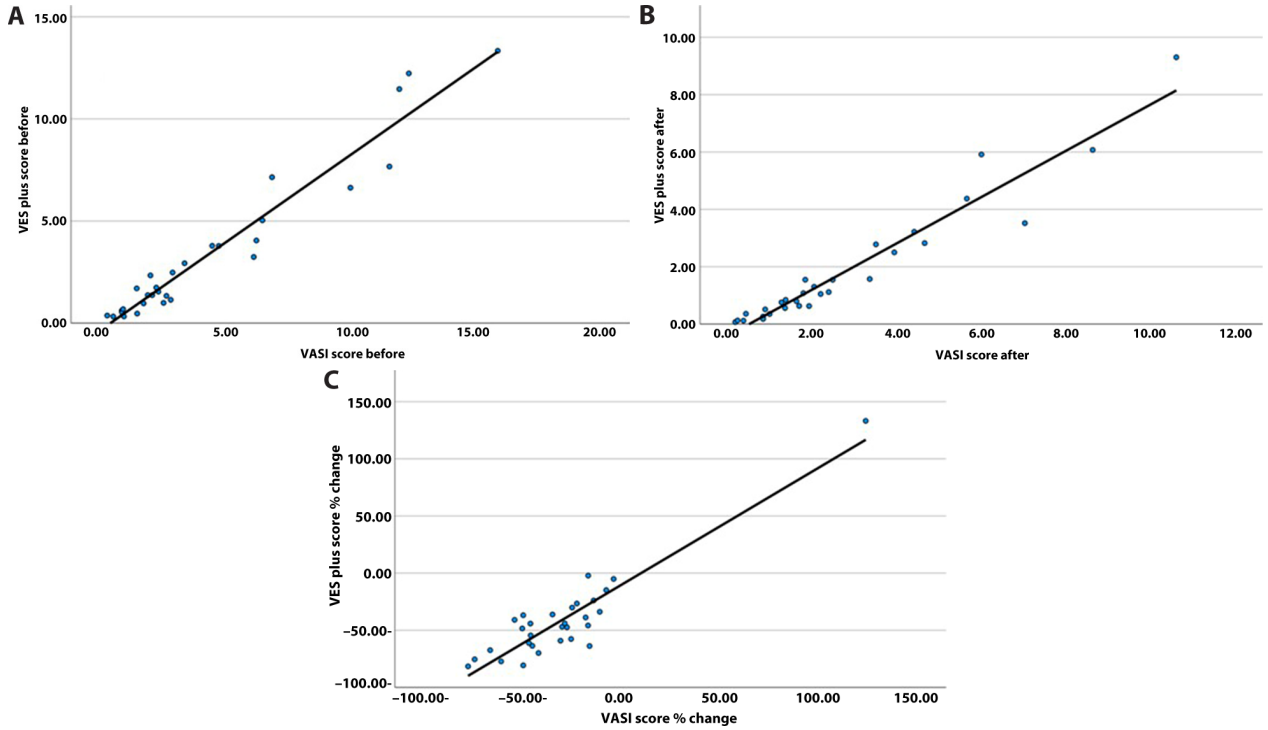

Figure 1. Strong Positive correlation between Vitiligo Extent Score plus (VES plus) and Vitiligo Area and Severity Index (VASI) scores both before and after narrow band Ultraviolet B (NB-UVB) treatment as well as percent change in the scores following treatment (r = 0.936, 0.97, 0.723).

On correlating both history-based VIDA score and examination based total VSAS, Koebner VSAS, hypochromic VSAS and confetti VSAS, none of the VSAS scores correlated with the VIDA score before NB-UVB treatment (r = - 0.007, -0.132, -0.106 and -0.015, respectively) (P = 0.97, 0.488, 0.576 and 0.938, respectively). Similarly, percent change in both scores did not correlate with one another (r = 0.03, -0.103, -0.005 and -0.140, respectively) (P = 0.876, 0.589, 0.98 and 0.462, respectively). After NB-UVB treatment, total, hypochromic and Koebner VSAS positively correlated with history-based VIDA score (r = 0.846, 0.873 and 0.427, respectively) (P < 0.001, < 0.001 and 0.018, respectively) (Figure 2). On the other hand, confetti VSAS did not correlate with VIDA score after NB-UVB treatment (r = 0.211, P = 0.263).

For assessing reliability of VES plus score in comparison to VASI, which is the most commonly used and cited extent score, reliability score was done for all readings of VES plus in comparison to VASI (both before and after treatment with NB-UVB) including the readings of the six patients who were dropped out making a total of 66 readings. It revealed an Intraclass Correlation Coefficient of 0.962 and Cronbach Alpha score of 0.981, P < 0.001 denoting high reliability of both scores (Table 2).

Conclusions

In the light of the challenging nature of vitiligo treatment [2], together with the diversity of the available tools for assessing treatment outcome [11], comparing the different available scores would help provide insights in their application. This, in turn, will aid in the process of unifying vitiligo assessment, which would help give way for a better analysis of different treatment modalities as well as comparing different clinical trials, which has currently been an urging need for the development of evidence -based recommendations for vitiligo [3-7].

When assessing vitiligo, both vitiligo activity and extent, together with lesional pigmentation are to be considered, where both pigmentation and cessation of spread of vitiligo are main treatment outcomes, from both patients' and physicians' perspectives [16]. Both VES plus [8] and VASI [9] scores consider extent and follicular pigmentation; thus, they stand as alternative tools, but the first is less time consuming, while the latter is most used. Regarding activity, VIDA [13], which is essentially history based, is the most used prior to the introduction of the VSAS [14], which is examination based. Thus, this work aimed at comparing the most recently developed vitiligo assessment tools for extent and activity in comparison to the most commonly used ones, at baseline, following treatment as well as their change with treatment.

In the current study, all scores have proven to change significantly with disease regression, which in turn points out to their utility as outcome measures for vitiligo follow up and comparison of different treatment modalities.

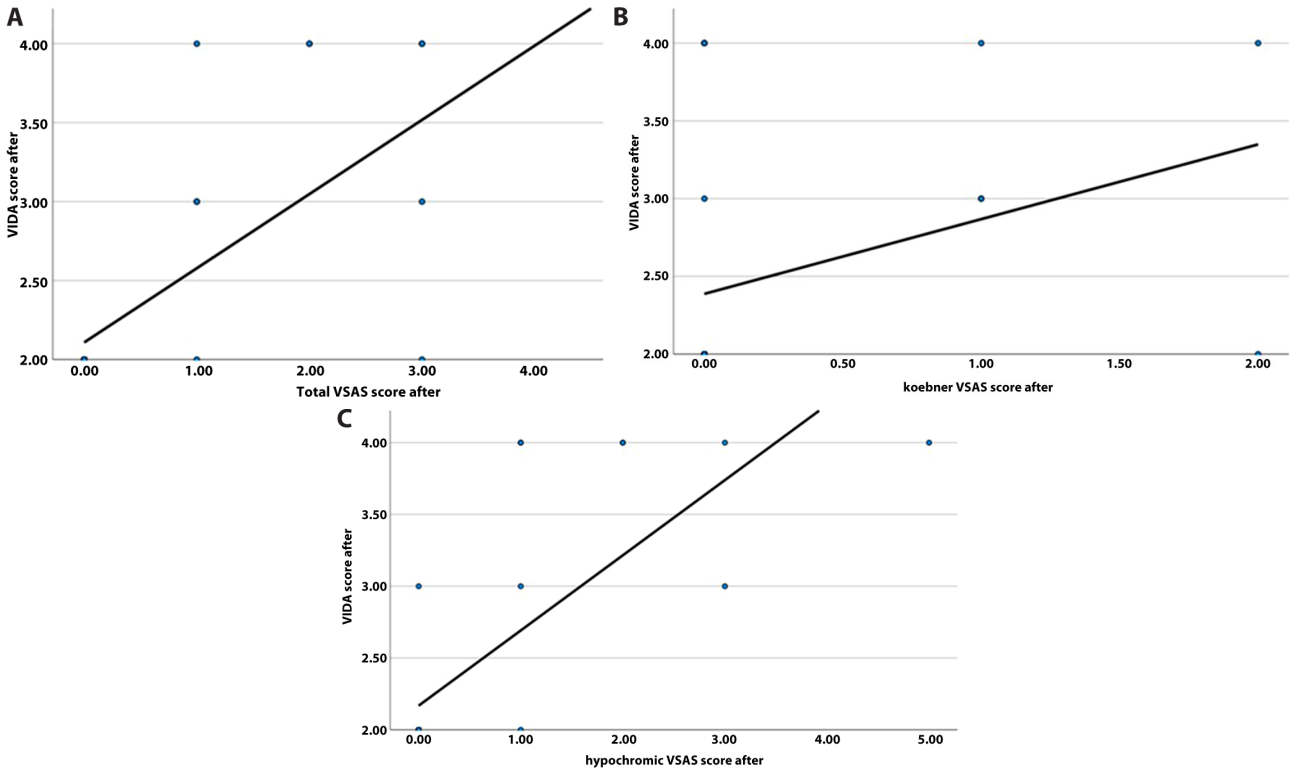

Figure 2. Positive correlation between Vitiligo Disease Activity Score (VIDA) and total, Koebner and hypochromic Vitiligo Signs Activity Score (VSAS) after narrow band Ultraviolet B (NB-UVB) treatment (r = 0.846, 0.427 and 0.873 respectively) (P < 0.001, 0.018 and < 0.001, respectively).

Table 2. Reliability of Vitiligo Extent Score Plus score in Comparison to Vitiligo Area and Severity Index score (N = 66).

		95% Confidence Interval		
	Value	Lower Bound	Upper Bound	P value
Intraclass Correlation Coefficient	0.962	0.939	0.977	<0.001
Cronbach alpha	0.981	0.968	0.988	<0.001

A significant positive correlation was detected between VES plus score and VASI before and after NB-UVB as well as their percent change following treatment. Additionally, both VES plus and VASI scores were found equally reliable. Thus, VES plus score stands as an easy, less time-consuming tool, to assess vitiligo extent taking into account perifollicular pigmentation which was one of the drawbacks of the original VES score [7,10].

Regarding activity scores, a significant positive correlation was detected between VIDA score and total VSAS score, Koebner VSAS and hypochromic VSAS after NB-UVB. However, VIDA score did not correlate with either VSAS scores before treatment with NB-UVB or with confetti VSAS after treatment.

To the best of our knowledge, no studies have yet compared VSAS to VIDA score. However, VIDA has been previously compared to VASI score, which have simulated patient reported activity to flipping a coin, due to lack of correlation to physician reported VASI score [17]. Since VIDA score is essentially history based [13], patients can easily miss activity especially prior to starting treatment when he is not much concerned about change in his disease. While on treatment, patients are more likely to be concerned about their disease and its progression which could explain why scores correlated only after treatment but not prior to treatment.

Regarding confetti VSAS, it did not correlate with VIDA neither before nor after treatment being a difficult clinical sign that patients are very likely to miss until the small macules coalesce in a well-recognized lesion. This highlights the fact that an examination-based assessment tool for vitiligo activity is indispensable to accurately identify vitiligo activity status and to meticulously follow up vitiligo activity.

In the context of vitiligo follow up and assessment of its dynamic change in terms of both pigmentation and activity, it is noteworthy to mention that Vitiligo Disease Activity Score (VDAS) and Vitiligo Disease Improvement Score (VDIS) have been recently introduced. Vitiligo Sings of Activity Score is suggested for a single point static assessment, while VDAS and VDIS scores for dynamic assessments on follow ups, where the same 15 body sites assessed in VSAS are reassessed for improvement (repigmentation) or worsening (activity) and scored accordingly [18]. However, this score is not readily available for implementation, but worth assessment and comparison to utilizing separate scores for assessing vitiligo extent and activity in the follow up.

Limitations to this study include failure to compare the newly developed semi-subjective scores; VES plus and VSAS to objective ones, which are essentially lacking for vitiligo activity. Additionally, our study has been conducted in a single tertiary center and all patients were either skin phototype III or IV. Thus, further studies involving larger cohorts as well as both active and stable vitiligo patients and different skin photo-types would help ascertain our findings.

Both VES plus and VSAS are effective tools for assessing vitiligo and its change with treatment, showing significant change with treatment similar to their widely used counterparts; VASI and VIDA scores. Being less time-consuming and user friendly, VES plus is privileged. For vitiligo activity, VSAS seems to address some of the missed signs of vitiligo activity, that can add to the accuracy of vitiligo activity status determination. Thus, VSAS will occupy an unprecedented position in vitiligo activity assessment, being the first to address different signs of vitiligo activity.

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