American Journal of Medicine and Medical Sciences 2022, 12(12): 1309-1318
DOI: 10.5923/j.ajmms.20221212.27

New Approaches to the Diagnosis of Vitiligo

Avaz Inoyatov, Nigora Khodjaeva, Shamsiddin Sadiev, Jakhongir Narziev

Republican Specialized Scientific and Practical Medical Center of Dermatovenerology and Cosmetology of the Ministry of Health of the Republic of Uzbekistan, Tashkent, Uzbekistan

Abstract The first mention of vitiligo was noted in the writings of Celsus and Seneca (1st century AD), however, even today, vitiligo cannot be completely cured, it is still a frequent violation of pigmentation, and its impact on the quality of life of patients is very important. According to experts of the British Association of Dermatologists (BAD), psychological distress in vitiligo is subject to screening evaluation. The purpose of the work: based on the use of calculators VAS, VASI and the study of the quality of life in patients to develop a scale for assessing the severity of vitiligo, taking into account the stage of the process, its prevalence, psychological distress of the patient. In addition to determining VES scores, the severity of the disease was judged on the VASI scale. As recommended, "according to the VASI scale, the calculation of the affected area is carried out according to the rule of the palms, since the area of the patient's palm is about 1% of the body surface, and the points are calculated as the area of the lesion expressed in the palms multiplied by the intensity of depigmentation (1 = complete depigmentation, 0.5 = 50% depigmentation)." Thus, our results showed that vitiligo debuted at a young age up to 30 years, in most cases it was generalized, progressive vitiligo was in 122 (42.5%) patients, the average duration of the disease was 42.6±3.6 months, and the severity of the lesion, estimated by M-VES and M-VASI, taking into account the quality of life, correlated with the VES and VASI scores, respectively, which indicates the validity of our proposed modifications of the scales for assessing the severity of vitiligo.

Keywords Vitiligo, Pigmentation - mexometry, VAS, NB-UVB

1. Introduction

The first mention of vitiligo was noted in the writings of Celsus and Seneca (1st century AD), however, even today, vitiligo cannot be completely cured, it is still a frequent violation of pigmentation, and its impact on the quality of life of patients is very important. According to experts of the British Association of Dermatologists (BAD), psychological distress in vitiligo is subject to screening evaluation. A lot of research and scientific papers have been conducted in the CIS countries and abroad on various aspects of the diagnosis and treatment of vitiligo, clinical recommendations on the establishment of clinical forms, stages and severity of vitiligo are constantly updated; recommendations of the European Dermatological Forum (2013), evaluation scales and calculators are proposed: VETF, VES, SA-VES, VASI scales [10,17,25,31], including with an emphasis on quality of life [7], however, there is no consensus on a single classification of vitiligo. To date, there is still insufficient clarity in determining the severity and activity of vitiligo, and evaluating the effectiveness of treatment is difficult due to the different methodological approach to the results obtained.

Establishing the severity of the process in vitiligo is a subject of discussion. First of all, visual assessment of lesions is carried out, determination of the level of pigmentation - mexometry, examination in the rays of a Wood lamp, UV photometry [23,24]. Several evaluation scales have been proposed: according to the Point-counting method; the palm method; according to the Vitiligo disease activity score (VIDA SCORE, 1999), the VASI scale (2004) [13], developed by analogy with PASI (Psoriasis area square) [15], EASI [4,5] VETF score (Vitiligo European task force, 2007); assessment of vitiligo severity index (Vitiligo extent tension index (VETI), 2014); VIPs [8,18,19], VIS-22 [11], VDAS [31], VSAS [28], photographing for monitoring, assessment of quality of life in vitiligo by VitiQoL, DLQL [9]. Computer modeling is also used in the programs AutoCAD 2000, PHOTOSHOP, COREL DRAW; spectrophotometry, confocal microscopy (reflectance confocal microscopy), a 3D method for assessing the lesion in vitiligo DIAS (Kawakami, 2011), a VES calculator (vitiligo extent score) [17] expressing the total skin lesion and its modifications – SA-VES (Naja van Geel) [29] and artificial intelligence [10,14,25,26,27].

Each of the proposed scales has its advantages and disadvantages. The VIDA scale has a number of limitations, because it takes into account the subjective opinion of the patient, does not take into account the prevalence of the process [22]. The VETF scale consists of three subscales (% area, staging 0-4, spreading -1-0-+1) and includes an assessment of the prevalence (rule of nines), the stage of the

Received: Nov. 30, 2022; Accepted: Dec. 20, 2022; Published: Dec. 23, 2022
Published online at http://journal.sapub.org/ajmms

disease (0-3 stages), the degree of progression (-1 - +1). The VETI scale takes into account the assessment of the affected area according to the rule of nines (similar to the assessment of the area of burns) multiplied by a coefficient. The VASI scale provides for the rule of palms to assess the prevalence of the process, since the area of the patient's palm is 1% of the body surface; the assessment of the degree of depigmentation on this scale is expressed in % (0-100%) [13]. At the same time, the degree of depigmentation is expressed as complete depigmentation -100%, single pigmented dots – 90%, depigmented and normal areas alternate with a predominance of depigmented – 75%, when the alternation of areas occurs equally – 50%, the predominance of normal zones over depigmented in one area – 25%, point depigmentation – 10% [12]. Recently, a VES scale, SA-VES, has been proposed, the tools of which allow to estimate the area of the lesion using computer visualization, as well as to take into account the degree of depigmentation. There are works where a correlation has been established between the VES and VASI estimates [3,14], which, according to most researchers, are currently the most optimal. At the same time, these scales do not take into account the patient's quality of life, and the VASI scale does not take into account the head and neck areas [21,30]. At the same time, it is important to emphasize that the presence of depigmentation on the face and neck causes a stronger psychological trauma than localization of the process in other parts of the body [16]. Some authors suggest multiplying the prevalence rate in these zones by 2 [1].

Even more difficult is the issue of evaluating the effectiveness of treatment for vitiligo. Thus, according to the results of a systematic review, 25 types of clinical outcomes of vitiligo are given in the literature, in 22% of the works the immediate results from the course of treatment were analyzed and repigmentation was detected in 96% of cases, and repigmentation was measured using 48 (!) different scales. Only 9% of the papers evaluated the quality of life, 13% of the papers contained information about the prevalence of the disease in the studied population, 17% of the papers studied patient satisfaction with treatment. Assessment of the quality of life of patients with vitiligo is important because the disease causes severe psychological trauma, up to depression, these patients feel stigmatized, experience violations of social adaptation [2,6], and psychological distress can aggravate vitiligo, cause the progression of depigmentation and hinder the achievement of a good result of treatment.

We believe that creating a universal index for vitiligo, which allows us to judge the prevalence, degree, stage, as well as evaluate the effectiveness of treatment and prognosis of vitiligo, is an important task. By analogy, a very convenient classification of TNM is used in oncology. Unfortunately, in dermatology today none of the methods is so simple and universal.

The purpose of the work: based on the use of calculators VAS, VASI and the study of the quality of life in patients to develop a scale for assessing the severity of vitiligo, taking into account the stage of the process, its prevalence, psychological distress of the patient.

2. Materials and Methods

There were 287 patients with non-segmental vitiligo (148 men and 139 women) aged 19-68 years who applied to the State Institution "RSNPMTSDVIK" in the period from 2018 to 2022. (table.1), the average age was 28.1±1.3 years.

Table 1. Distribution of patients by age and gender

Age, years	M		F		Overall	
	n	%	n	%	n	%
19-45	109	73,6	116	83,6	225	78,4
45-59	21	14,2	15	10,8	36	12,5
60-74	18	12,2	8	5,6	26	9,1
Overall	148	100	139	100	287	100

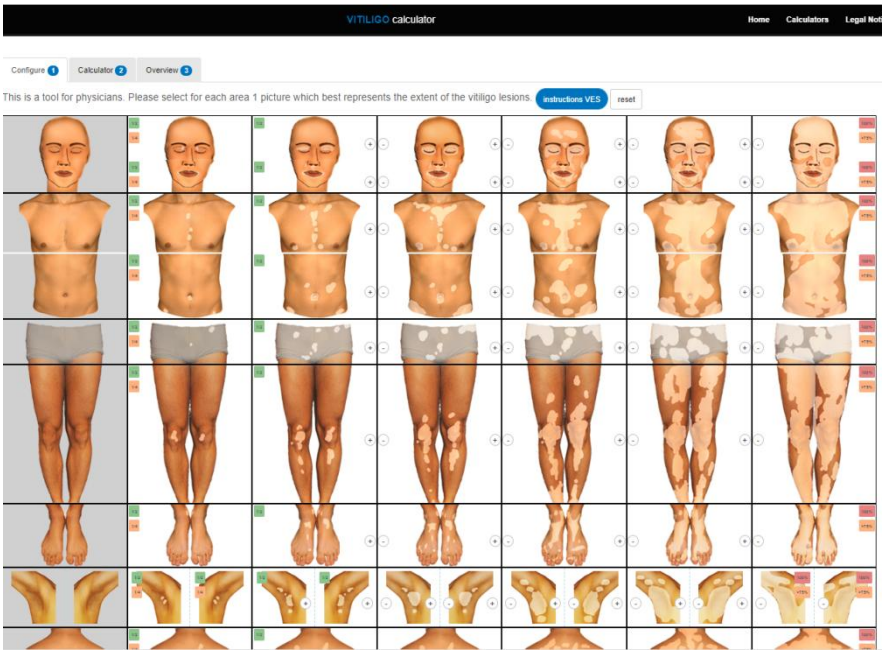
The evaluation of the prevalence of the process using the VES calculator was carried out using the application (https://www.vitiligo-calculator.com). The calculator provides an estimate, which can be expressed as a percentage of the involvement of the body surface area (BSA) or the degree of spread to the area (from 0 to 6), you need to choose a suitable pattern for the affected area, and also note the degree of depigmentation, also according to the pigmentation scale (Fig. 1).

In addition to determining VES scores, the severity of the disease was judged on the VASI scale. As recommended, "according to the VASI scale, the calculation of the affected area is carried out according to the rule of the palms, since the area of the patient's palm is about 1% of the body surface, and the points are calculated as the area of the lesion expressed in the palms multiplied by the intensity of depigmentation (1 = complete depigmentation, 0.5 = 50% depigmentation)." The calculation on the VASI scale consists of the total amount of points for the severity of the lesion on the body, arms, hands, body, lower limbs, feet (Fig. 2).

The assessment of the quality of life was carried out according to DIKZH.

We also developed a modification of VAS, VASI and evaluated their validity - we conducted a comparative analysis of the severity of vitiligo on the VASI, M-VASI, VES, M-VES scales.

The degree of progression of the disease was determined by the presence of the following signs, allowing to distinguish a stable disease from a progressive one. Signs of ongoing depigmentation include: 1) Indistinct boundaries of foci or the appearance of new point depigmented areas, 2) Kebner phenomenon, 3) "Trichromic" staining in foci, 4) Signs of inflammation, hyperemia and itching in foci [20].

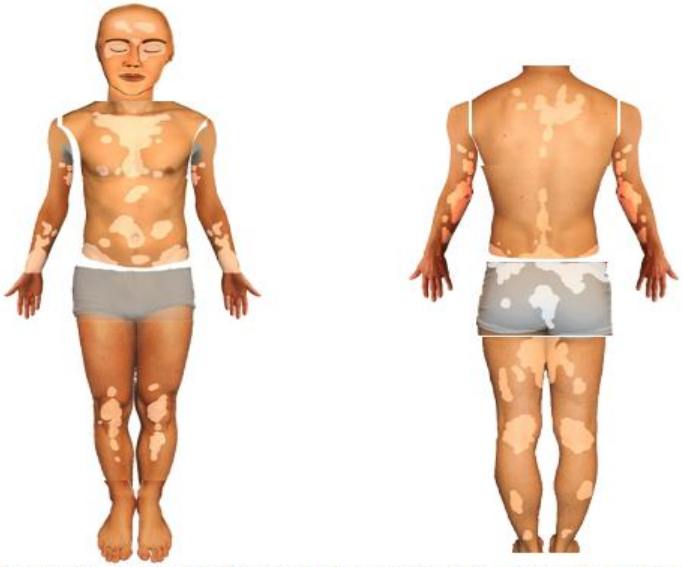


www.vitiligo-calculator.com online VES calculator

CODE/reference number:

Bodypart	BSA	Grade
Face (upper)	0,5625	4
Face (lower)	0	0
Trunk (upper)	2	4
Trunk (lower)	2	4
Waist	0	0
Legs (front)	1,4	3
Feet	0	0
Axilla (right)	0	0
Axilla (left)	0	0
Back (upper)	0,8	3
Back (lower)	0,8	3
Gluteal	1	4
Legs (back)	4	4
Hand (left)	0	0
Hand (right)	0	0
Arm (front, right)	0,875	4
Arm (back, left)	0,875	4
Arm (front, left)	0,875	4
Arm (back, right)	0,875	4
Total	16,0625	

Region	BSA
Face	0,5625
Trunk (including front and back side trunk and waist)	6,6
Extremities (including legs, arms, axillae)	8,900
Feet	0
Hands (left & right)	0
Total VES score	16,0625



This document was generated automatically on 27-10-2022 07:35:47 by the VES-calculator available online at www.vitiligocalculator.com. Remark: composition of this figure is based on the pictures included in the calculator per category (0-6). © 2022. VES calculator. All rights reserved

Figure 1. VES view

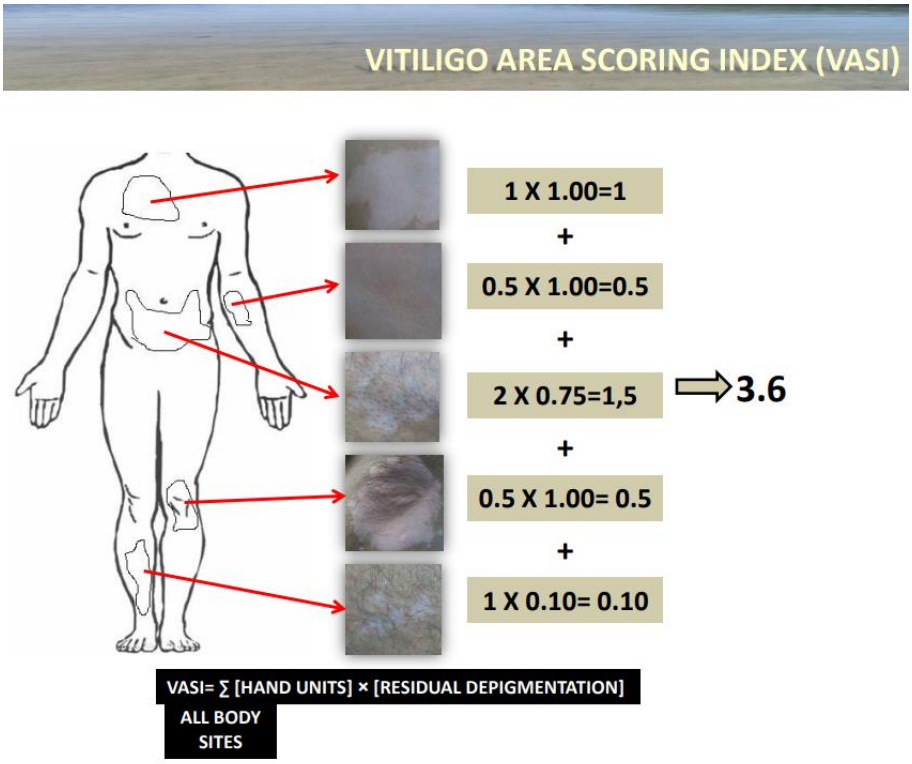


Figure 2. VASI score

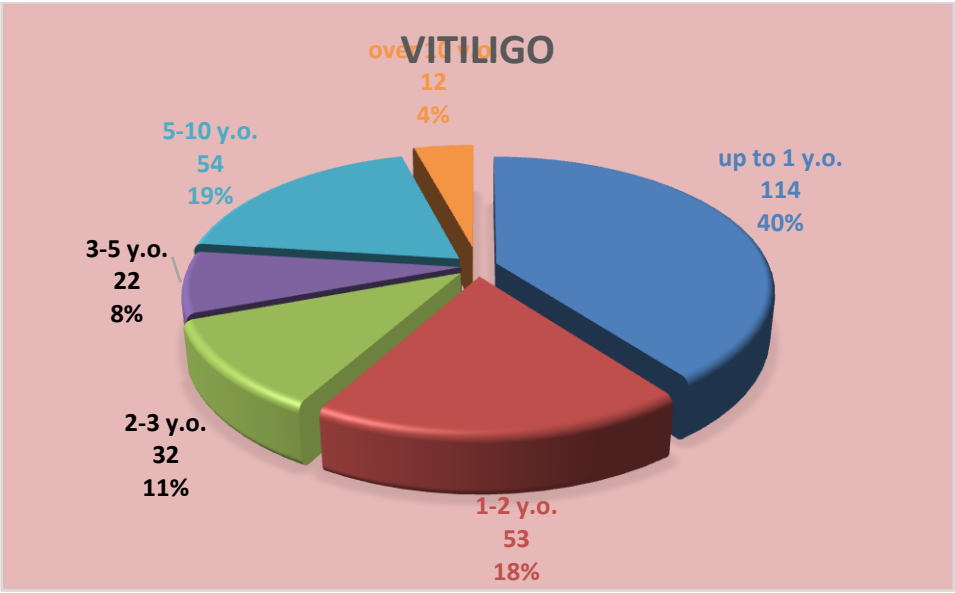


Figure 3. Distribution of patients depending on the age of vitiligo onset

3. Results and Discussion

All our patients were with segmental vitiligo. The duration of the disease averaged 42.6±3.6 months, while the onset of vitiligo for less than 1 year before treatment was in 114 patients (40%), the duration up to 2 years – in 53 (18%), from 2 to 5 years – in 54 (18.8%), 5-10 years – 54 (18.8%) (fig. 3).

The differential diagnosis was performed with post-inflammatory hyperpigmentation, piebaldism, idiopathic hypopigientation, focal scleroderma, scleroatrophic lichen, white lichen, chemical leukoderma, the initial stage of leprosy and multicolored lichen.

The degree of progression was assessed by a set of clinical signs proving the instability of the course of vitiligo – i.e., the tendency to increase foci, the appearance of new foci, as well as the presence of scalloped vitiligo, tricolor staining of foci and signs of inflammation in the foci. In the presence of these components, we considered vitiligo unstable, progressive, and conditionally designated as (+1), stable vitiligo we

designated as (0), and regressive, i.e. with a tendency to repigmentation and reduction of the area of foci – as (-1) (Fig. 4).

Unstable vitiligo was detected in 122 (42.5%) patients. The activity of the process (unstable course) was characterized by the presence of all 3 signs: "scalloped" vitiligo, tricolor vitiligo, the presence of the Kebner phenomenon in 85 (29.6%) patients, an increase in the area of existing foci and the appearance of new ones during the last 3 months was in 33 (11.5%) patients, in 4 (1.4%) cases there was the process of inflammation in the foci was revealed. Vitiligo is stable in 165 (57.5%).

Note that the existing VETF scale provides an assessment of three components: prevalence (% area), severity (0-4) (staging), as well as the degree of progression (spreading (-1) – (+1). The authors recommend evaluating these signs on 5 areas of the body separately, which, in our opinion, is not advisable regarding the assessment of the progression of the process. As our observations show, if there is a progression in at least one of their depigmentation sites, treatment tactics change towards limiting indications for phototherapy with the appointment of exclusively NB-UVB (311nm) therapy and minipulse therapy of GCS [12]. Based on this, we believe that the statement of instability of vitiligo (progressive course) may be valid even if there are signs in 1 focus.

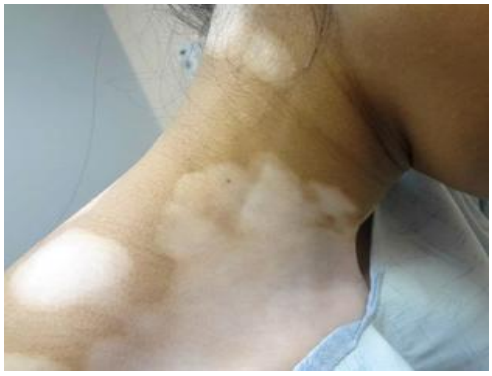
Depending on the form of the disease, we found no significant differences in the number of patients with stable and unstable vitiligo (Table 2).

Table 2. Distribution of patients depending on vitiligo activity

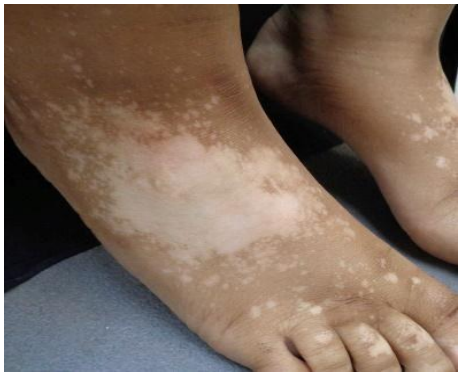
Clinical form	Stable (0)	Unstable (+1)	Overall
Generalized, n	120	87	**207**
Acrofacial, n	29	23	**52**
Universal, n	3	2	**5**
Mixed, n	9	8	**17**
Vitiligo of the mucous membranes, n	4	2	**6**
Rare species	0	0	**0**
Overall	**165**	**122**	**287**

*-statistically significant relative to the generalized form

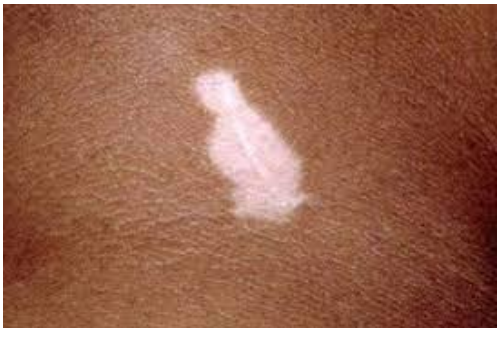
The assessment of the quality of life in 287 patients with non-segmental vitiligo showed that the rate of DIC strongly depends on the localization of depigmentation foci, as well as on the duration of the disease: people with a long-standing process have a calmer attitude to the disease and consider the quality of life to be moderately reduced than patients with newly emerged vitiligo who experience severe emotional distress. Also, the quality of life was significantly lower in patients with progressive vitiligo (Fig. 5).



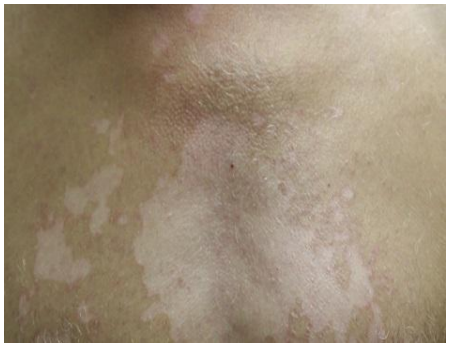
Tricolor vitiligo



"Scalloped" vitiligo



The Kebner phenomenon (pigmentation around the injury)



The process of inflammation

Figure 4. Signs of unstable course of vitiligo

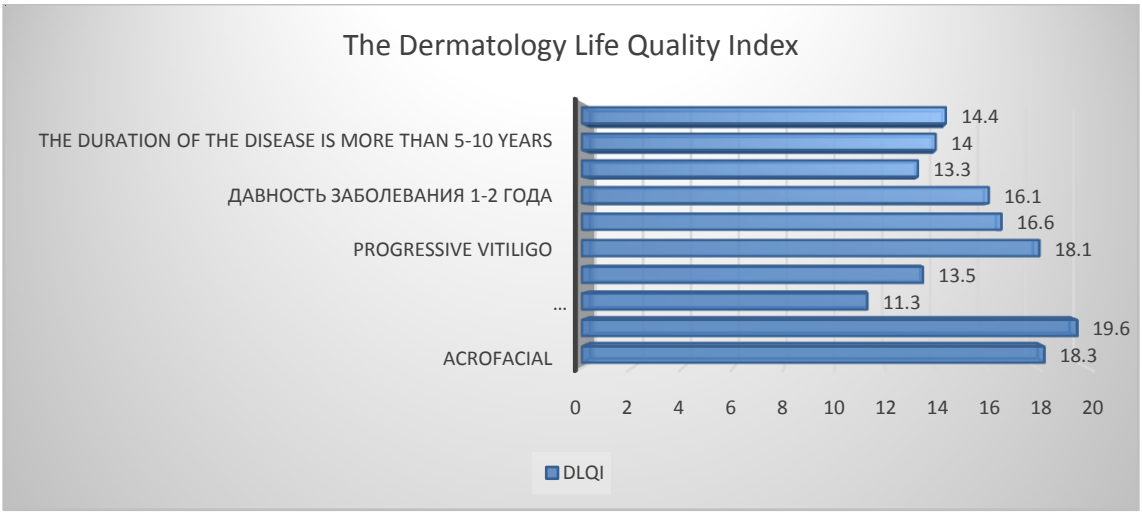


Figure 5. Quality of life (according to DIKZH) in persons with vitiligo

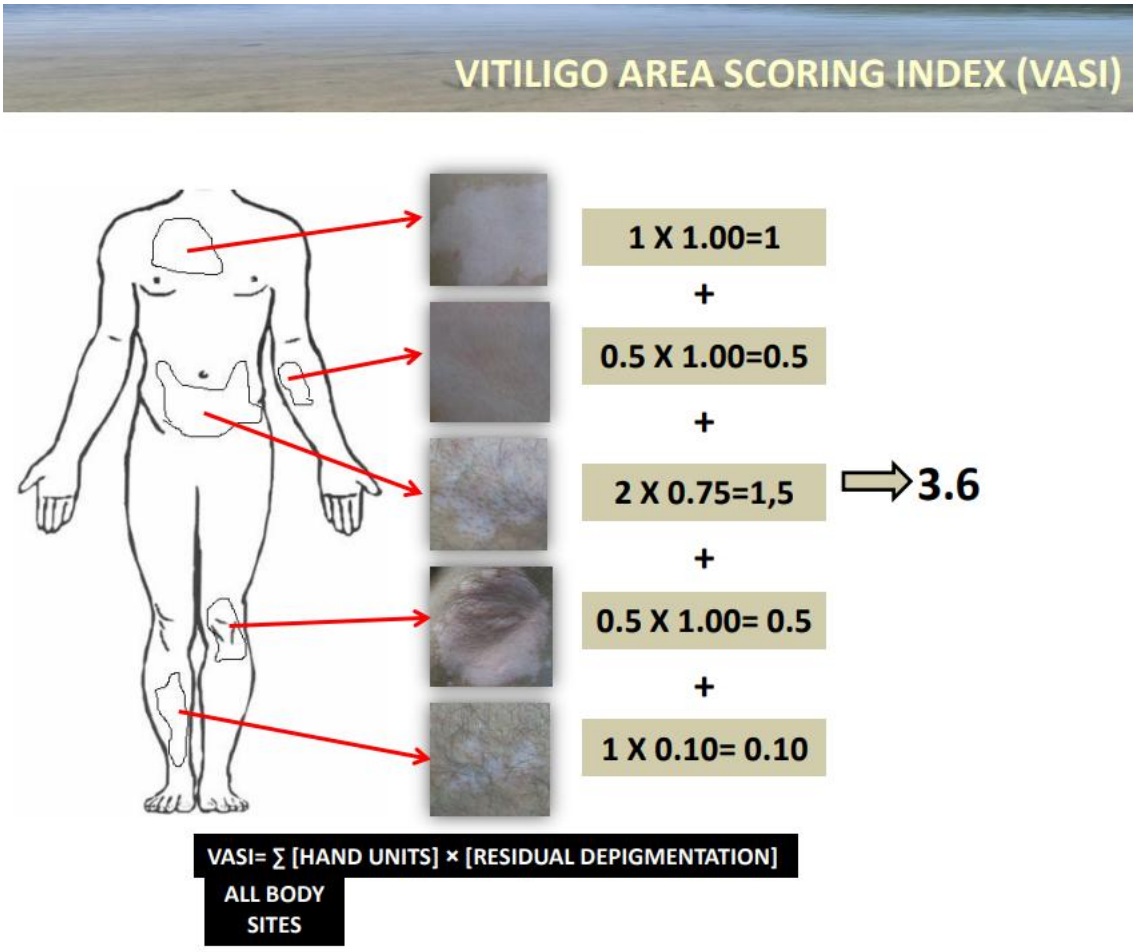


Figure 6. Calculation of the VASI score

As can be seen from Fig. 5, there were significant differences in the DIQF parameter depending on the presence of facial lesions: 19.6±0.4 points versus 11.3±0.2 ($p<0.05$), i.e. in patients with localization of lesions on the face, the DIQF was 1.7 times higher ($p<0.05$).

In patients with disease progression, the LVI was also 1.4 times higher than in stable vitiligo: 18.1±0.5 versus 13.5±0.4 points ($p<0.05$). The causal relationships of this are difficult to uncover, because a vicious circle arises: stress – depigmentation – stress – progression of vitiligo - stress. Perhaps this is due to the fact that emotions are the sum of endocrine–autonomic reactions, and the central nervous and autonomic nervous systems interact very closely with the immune system at the level of neurotransmitters,

inflammatory mediators and growth factors. It should be noted that in the recommendations of the British Association of Dermatologists (BAD), compiled on the basis of an analysis of existing publications on vitiligo (9600 papers, of which 13 systematic reviews), the recommendation "screening of all patients with vitiligo for the level of psychological distress during the initial examination and evaluation" is in the first place. It is important to attach importance to the assessment of the psychoemotional state of the patient, his autonomic regulatory system. Based on the results obtained by us on the study of DIC in patients with vitiligo, we propose to include this indicator in the existing assessment scales of vitiligo severity – in the VES, VASI scale.

Our results of assessing the severity of vitiligo by VASI showed that the average score was 4.22±0.73, while the minimum value was 1.3, and the maximum was 8.5 points. As recommended, "according to the VASI scale, the calculation of the affected area is carried out according to the rule of the palms, since the area of the patient's palm is about 1% of the body surface, and the points are calculated as the area of the lesion expressed in the palms multiplied by the intensity of depigmentation (1 = complete depigmentation, 0.5 = 50% depigmentation)." The calculation on the VASI scale consists of the total amount of points for the severity of the lesion on the body, arms, hands, body, lower limbs, feet (Fig. 6).

At the same time, this scale does not take into account the lesion of the face and hands, as well as the level of psychoemotional distress.

The modification of the VASI scale (M-VASI) developed by us included the introduction of another component – the "face" and coefficients for recalculating the indicator when the process is localized on the face and hands: the coefficient is 2, because according to the quality of life questionnaire of the DIKJ, we found that the quality of life with such localization of the process is 1.7-2.0 times lower than in other patients with vitiligo.

So, the calculation on the VASI scale looks like this: VASI = hand score + hand score + body score + lower limb score + foot score.

The calculation on the M-VASI scale looks like: M-VASI = (score face*2) + hand score + (brush score*2) + body score + lower limb score + foot score.

The evaluation of the M-VASI indicators showed that the average score increased due to the introduced coefficients and amounted to 5.32 ± 0.97, the minimum value was 1.75, the maximum was 10.9 points. There were no significant differences between VASI and M-VASI ($p>0.05$). The correlation coefficient of M-VASI with the VASI scale was $r=0.992$ ($p<0.0001$), which characterizes the relationship as strong, direct, reliable and proves the informativeness of M-VASI, comparable to that of the generally accepted VASI scale. At the same time, the correlation coefficient of M-VASI with the DIKJ scale was $r=0.455$ ($p<0.05$), which characterizes the relationship as a reliable straight line of average strength, while there was no correlation of the VASI indicator with the DIKJ (at $r=-0.196$, $p=0.674$).

The VASI, M-VASI indicators, depending on the form of the disease, were distributed as follows (Table 3).

Table 3. Indicators for VASI, M-VASI, DIKJ in patients with vitiligo

Form of vitiligo	VASI	M-VASI	DK
Generalized	7,4±0,5	8,9±0,9	16,0±1,2
Acrofacial	4,25±0,4*	6,25±0,4*	18,3±0,7
Universal	5,1±0,4*	5,1±0,3*	16,1±0,5
Mixed	5,3±0,2*	4,9±0,2*	12,0±0,3*
Vitiligo of the mucous membranes	2,7±0,2*	2,8±0,2*	8,0±0,3*
In all patients	4,22± 0,73	5,32±0,97	14,4±0,8

*- statistically significant relative to the generalized form at $p<0.05$.

Thus, these results indicate that the modified M-VASI scale, on the one hand, correlates with the DIQ, which cannot be said about VASI, and on the other hand, there is no significant difference between VASI and M-VASI, i.e. M-VASI does not distort the result of assessing the area and severity of depigmentation, calculated according to VASI, moreover, due to the presence of a correlation with DIC, M-VASI also reflects the quality of life of the patient.

Our proposed modification of VES consisted in summing the BSA indicator, calculated automatically by a computer program, and the score on the DIKJ: M-VES=VES+DIKJ.

As our observations showed, the average score on the VES scale was 13.8±7.5, with minimum values of 0.91 points and maximum values of 55.8 points with 95% CI: 4.43-32.01 points. The wide range of fluctuations in VES scores is due to the fact that in generalized vitiligo this indicator is significantly higher than in acrofacial ($p<0.05$). At the same time, the quality of life, as we noted earlier, deteriorated most severely in the acrofacial type, as well as in generalized vitiligo with facial lesions, as evidenced by the high score on DIQ in these patients. We propose to summarize the scores on 2 scales: VES and DIKJ for a full assessment of the severity of vitiligo (Table 4).

Table 4. Indicators for VES, VES in patients with vitiligo

Form of vitiligo	VES	M-VES
Generalized	12,5± 3,3	34,0±6,6
Acrofacial	3,43±0,13*	18,8±4,3*
Universal	19,5±0,9*	28,3±3,3
Mixed	4,2±0,8*	12,5±1,3*
Vitiligo of the mucous membranes	4,1±0,3*	9,0±1,0*
In all patients	13,8±7,5	28,3±6,9

*- statistically significant relative to the generalized form at $p<0.05$.

The average score on the M-VES scale, which takes into account the quality of life, was 34.0±6.6 for generalized and 18.8±4.3 for acrofacial, which does not differ statistically significantly, because the quality of life in patients with localization of foci on the face is significantly worse than in

other forms of vitiligo.

Correlation analysis of VES and M-VES showed the presence of a direct strong connection at r=0.954, p=0008; the VES/DIKJ connection was weak, unreliable r=0.231, p=0.219; whereas the M-VES/DIKJ connection was of average strength and reliable at r=0.531, p=0.045. These results It is shown that M-VES strongly correlates with VES, i.e. it does not distort the result of VES, and also takes into account the quality of life of the patient.

We believe that taking into account the quality of life is crucial in assessing the severity of vitiligo, because the patient's quality of life depends on the degree of pigmentation restoration and skin color leveling, how he evaluates the effect of treatment. Also, patients with vitiligo with a reduced quality of life according to DIKZH (a total score of more than 15) need to consult a psychologist / psychotherapist to exclude psychosomatic manifestations in vitiligo.

Thus, our results showed that vitiligo debuted at a young age up to 30 years, in most cases it was generalized, progressive vitiligo was in 122 (42.5%) patients, the average duration of the disease was 42.6±3.6 months, and the severity of the lesion, estimated by M-VES and M-VASI, taking into account the quality of life, correlated with the VES and VASI scores, respectively, which indicates the validity of our proposed modifications of the scales for assessing the severity of vitiligo.

The quality of life in patients with vitiligo was sharply reduced (by 11-19 times relative to those without vitiligo), amounting to 14.4±0.8 points versus 1.5±0.2 in the control group. At the same time, there was a significant difference in the index of DIC depending on the form of the disease, when in persons with localization of the lesion on the face, the DIC was 19.6 ± 0.4 points versus 11.3 ± 0.2 points in the generalized form without facial lesion. This shows that with the localization of depigmentation foci on the face and palms, the index of DIC is significantly higher, and the quality of life is significantly lower than with other forms of vitiligo. The quality of life in patients with vitiligo correlated with the score on the M-VES and M-VASI scales, and the correlation of the VASI/M-VASI and VES/M-VES scales was reliable, strong direct with a correlation coefficient of r= 0.99 and r=0.95, respectively. This indicates the comparability of the scales modified by us with the generally accepted ones, does not distort their results. The M-VES and M-VASI scales modified by us also have the advantage of reflecting the quality of life of patients with vitiligo and can be used to assess the outcome of treatment.

4. Conclusions

1. The quality of life in patients with vitiligo according to DIKJ was 14.4±0.8 points versus 1.5±0.2 in the control group ($p<0.05$); there was a significant difference in the DIKJ index depending on the form of the disease, when in persons with localization of the lesion on the face DIKJ was 19.6±0.4 points versus 11.3±0.2 points with generalized form without facial lesion ($p<0.05$).

2. The indicator on the VES scale correlated weakly and unreliably with the DIC at r=0.231, p=0.219; the VASI indicator correlated with the DIC at r=-0.196, p=0.674, which indicates unreliable weak connections and indicates the absence of a relationship.

3. The modified M-VASI and M-VES scales correlated with the DIC at r=0.455 ($p<0.01$) and r=0.531 ($p<0.01$), respectively, which indicates a direct relationship with the average.

4. The modified M-VASI and M-VES scales do not distort the result of the assessment of the area and severity of depigmentation calculated by VASI and VES respectively, as evidenced by the correlation of VASI/M-VASI and VES/M-VES at r= 0.99 ($p<0.01$) and r=0.95 ($p<0.01$) accordingly.

REFERENCES

[1] Bhargava P, Prakash C, Tiwari S. Correlating melanin index to repigmentation potential: A novel prognostic tool in vitiligo // Pigment Int 2016; 3: 72–6.

[2] Bibeau K., A.G. Pandya, K. Ezzedine, H. Jones, J. Gao, A. Lindley, J.E. Harris. Vitiligo prevalence and quality of life among adults in Europe, Japan and the USA // Journal of the European Academy of Dermatology and Venereology. -2022. -Volume 36, Issue 10.

[3] Chandrashekar BS, N Shobha, P Jagadish, Vani Vasanth, ML Rajashekar, MA Sandeep 308 nm excimer lamp in combination with topical tacrolimus: A retrospective study of its efficacy and safety in childhood vitiligo // Indian J Paediatr Dermatol 2014;15:74-8.

[4] Chopra R, Vakharia PP, Sacotte R. Severity strata for Eczema Area and Severity Index (EASI), modified EASI, Scoring Atopic Dermatitis (SCORAD), objective SCORAD, Atopic Dermatitis Severity Index and body surface area in adolescents and adults with atopic dermatitis // Br J Dermatol 2017; 177: 1316–1321.

[5] Chopra R, Vakharia PP, Simpson EL, Paller AS, Silverberg JI. Severity assessments used for inclusion criteria and baseline severity evaluation in atopic dermatitis clinical trials: a systematic review // J Eur Acad Dermatol Venereol 2017; 31: 1890–1899.

[6] Dabas G., K. Vinay, D. Parsad, A. Kumar, M.S. Kumaran. Psychological disturbances in patients with pigmentary disorders: a cross-sectional study // Journal of the European Academy of Dermatology and Venereology. -2019. -Volume 34, Issue 2. First published: 30 September 2019.

[7] Elbuluk N, Ezzedine K. Quality of life, burden of disease, co-morbidities, and systemic effects in vitiligo patients // Dermatol Clin. 2017; 35(2): 117–28.

[8] Ezzedine K, Ahmed M, Tovar-Garza A. Cross-cultural validation of a short-form of the Vitiligo Impact Patient scale (VIPs) // J Am Acad Dermatol 2019; 81: 1107–1114.

[9] Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) – a simple practical measure for routine clinical use// Clin Exp Dermatol 1994; 19: 210–216.

[10] Guo L, Yang Y, Ding H, Zheng H, Yang H, Xie J, Li Y, Lin T, Ge Y. A deep learning-based hybrid artificial intelligence model for the detection and severity assessment of vitiligo lesions// Ann Transl Med. 2022 May; 10(10): 590. doi: 10.21037/atm-22-1738. PMID: 35722422 Free PMC article.

[11] Gupta V, Ramam M. Vitiligo Impact Scale (VIS)-22: A measure of the psycho-social burden of vitiligo // Indian J Dermatol Venereol Leprol 2022; 88: 691-695.

[12] Hamzavi I, Jain H, McLean D, Shapiro J, Zeng H, Lui H. Parametric modeling of narrowband UV-B phototherapy for vitiligo, using a novel quantitative tool: the Vitiligo Area Scoring Index. //Arch Dermatol. 2004; 140: 677–683.

[13] Kitchen Helen, Kathleen W Wyrwich, Chloe Carmichael, Linda S Deal , Tatjana Lukic , Tamara Al-Zubeidi, Chris Marshall, Hannah Pegram, Iltefat H Hamzavi, Brett King. Meaningful Changes in What Matters to Individuals with Vitiligo: Content Validity and Meaningful Change Thresholds of the Vitiligo Area Scoring Index (VASI) // Dermatol Ther (Heidelb). - 2022 Jul; 12(7): 1623-1637. doi: 10.1007/s13555-022-00752-8. Epub 2022 Jun 30.

[14] Mogawer Rania M, Wedad Z Mostafa[1], Maha Fathy Elmasry Comparative analysis of the body surface area calculation method used in vitiligo extent score vs the hand unit method used in vitiligo area severity index // J Cosmet Dermatol 2020 Oct; 19(10): 2679-2683. doi: 10.1111/jocd.13311. Epub 2020 Feb 3.

[15] PASI Calculator. http://pasi.corti.li/Psoriasis Area Severity Index (PASI) Calculator (1.7.1). Accessed December 30, 2013).

[16] Patel K.R., V. Singam, S. Rastogi, H.H. Lee, N.B. Silverberg, J.I. Silverberg Association of vitiligo with hospitalization for mental health disorders in US adults //Journal of the European Academy of Dermatology and Venereology. -2018. -Volume 33, Issue 1.

[17] Pichanee Ch, Silpa-Archa N., Apinuntham Ch [1], Chaiyabutr Chayada[1], Chanisada Wongpraparut Reliability, Validity and Feasibility of the Vitiligo Extent Score (VES) and Self-Assessment Vitiligo Extent Score (SA-VES) Among Vitiligo Patients: A Cross-Cultural Validation // Clin Cosmet Investig Dermatol. - 2021 Jul 28; 14: 949-957. doi: 10.2147/CCID.S324073. eCollection 2021

[18] Salzes C, Abadie S, Seneschal J, Whitton M, Meurant J-M. TheVitiligo Impact Patient scale (VIPs): development and validation of a vitiligo burden assessment tool // J Investig Dermatol.2017.-136(1):52– 58.

[19] Shourick J., J. Seneschal N. Andreu J.-M. Meurant, I. Pane, P. Ravaud, V.-T. Tran, K. Ezzedine Vitiligo Treatment Impact score (VITs): development and validation of a vitiligo burden of treatment questionnaire using the ComPaRe Vitiligo e-cohort // First published: 17 October 2021 https://doi.org/10.1111/jdv.17742 1.

[20] Speeckaert R., J. Dugardin, J. Lambert, H. Lapeere, E. Verhaeghe, M.M. Speeckaert, N. van Gee. Critical appraisal of the oxidative stress pathway in vitiligo: a systematic review and meta-analysis // Journal of the European Academy of Dermatology and Venereology.-2018.-Volume 32, Issue 7.

[21] Taïeb A., J.-M. Meurant Should we prioritize psychological interventions in the management of vitiligo? // Journal of the European Academy of Dermatology and Venereology. -2018. -Volume 32, Issue 12.

[22] Taïeb A., Picardo M. The definition and assessment of vitiligo: a consensus report of the Vitiligo European Task Force // Pigment Cell Res. -2007; 20: 27–35.

[23] Uitentuis S.E., M.N. Heilmann, R.M. Verdaasdonk, J.M. Bae, R.M. Luiten, A. Wolkerstorfer, M.W. Bekkenk. Ultraviolet photography in vitiligo: image quality, validity and reliability // Journal of the European Academy of Dermatology and Venereology.-2020.-Volume 34, Issue 7.

[24] Uitentuis S.E., M.W. Bekkenk, N. van Geel, M.A. de Rie, A. Wolkerstorfer. UV light set-ups for vitiligo photography, a comparative study on image quality and ease of use // Journal of the European Academy of Dermatology and Venereology.-2019.-Volume 33, Issue 10.

[25] van Geel N, Bekkenk M, Lommerts JE, Ezzedine K, Harris J, Hamzavi I, Eleftheriadou V, Picardo M, Taieb A, Prinsen CA, Wolkerstorfer A, Speeckaert R.The Vitiligo Extent Score (VES) and the VESplus are responsive instruments to assess global and regional treatment response in patients with vitiligo // J Am Acad Dermatol. 2018 Aug; 79(2): 369-371.

[26] van Geel N, Lommerts J, Bekkenk M, Wolkerstorfer A, Prinsen CA, Eleftheriadou V, Taïeb A, Picardo M, Ezzedine K, Speeckaert R. Development and Validation of the Vitiligo Extent Score (VES): an International Collaborative Initiative // J Invest Dermatol. 2016 May; 136(5): 978-84.

[27] van Geel N, Lommerts JE, Bekkenk MW, Prinsen CA, Eleftheriadou V, Taieb A, Picardo M, Ezzedine K, Wolkerstorfer A, Speeckaert R; international Vitiligo Score Working Group. Development and validation of a patient-reported outcome measure in vitiligo: The Self Assessment Vitiligo Extent Score (SA-VES) //J Am Acad Dermatol. 2017 Mar; 76(3): 464-471.

[28] van Geel N, Passeron T, Wolkerstorfer A, Speeckaert R, Ezzedine K. Reliability and validity of the Vitiligo Signs of Activity Score (VSAS) // Br J Dermatol. -2020 Nov; 183(5): 883-890.

[29] van Geel N, Uitentuis SE, Zuidgeest M, Wolkerstorfer A, Bekkenk MW, Moock C, Van Goethem C, Verlaeckt E, Smet C, Grine L, Speeckaert R. Validation of a Patient Global Assessment for extent, severity and impact to define the severity strata for the Self Assessment Vitiligo Extent Score (SA-VES) // J Eur Acad Dermatol Venereol. 2021 Jan; 35(1): 216-221.

[30] van Geel N, Wolkerstorfer A, Lommerts JE, Ezzedine K, Eleftheriadou V, Hamzavi I, Harris J, Picardo M, Taieb A, Prinsen CAC, Bekkenk M, Speeckaert R. Validation study of the Vitiligo Extent Score-plus // J Am Acad Dermatol. 2018 May; 78(5): 1013-1015.

[31] van Geel N., L. Depaepe, V. Vandaele, L. Mertens, J. Van Causenbroeck, S. De Schepper, L. Van Coile, A. Van Reempts, A.-S. De Vos, J. Papeleu, I. Hoorens, D. Mertens, A. Wolkerstorfer, J.E. Lommerts, R. Speeckaert Assessing the dynamic changes in vitiligo: reliability and validity of

the Vitiligo Disease Activity Score (VDAS) and Vitiligo Disease Improvement Score (VDIS) // Journal of the European Academy of Dermatology and Venereology. -2022. -Volume 36, Issue 8.