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THE METHOD FOR PREDICTIVE ASSESSMENT OF THE CONDITION OF PATIENTS WITH ATOPIC DERMATITIS AT DIFFERENT STAGES OF THE DISEASE

The **subject** of the research is the development of a method for prognostic assessment of the condition of patients with atopic dermatitis at different stages of the disease. The **goal** of the work is to study the informativeness of immunological indicators and data from dermatoscopic examinations in order to expand the possibilities of prognostic objectification of methods for assessing the condition of patients with atopic dermatitis with varying degrees of severity of the disease. The **task** of the work includes objectifying the blurring of assessment standards when analyzing the transition from one stage of the disease to another. **Methods.** The solution to this problem is possible when assessing the possibility of using models of parametric recognition (discrimination) using indicators of immunoglobulins in blood serum and indicators of immunograms, as well as color characteristics of skin areas based on the analysis of dermatoscopic images at various degrees of severity of the disease. **Result.** In the course of the study, the analysis of the color characteristics of the skin showed that when immunological blood parameters are added to the discrimination model, the probability of an error in making prognostic decisions significantly decreases. Predictive assessment of the condition of a patient with atopic dermatitis only by the color characteristics of the skin makes it possible to control this pathology with a higher degree of probability, which makes it possible to use the digital dermatoscopy method independently for express objectification of the condition of a patient with atopic dermatitis without waiting for the data of immunological analyzes. When a new patient appears, the above indicators are calculated for him and the normalized Euclidean distances to the center of the clusters corresponding to the studied pathologies are calculated. The calculated distances can be ranked and the probabilities of correspondence of the given case to specific pathologies can be determined. **Conclusions.** The prospect of further work is to substantiate the metrological characteristics of the method to eliminate possible systematic errors associated with the method of obtaining optical information.

Keywords: atopy; dermatitis; luminance channel; dermatoscopy; discrimination pattern.

Formulation of the problem

Atopic dermatitis (AD) is a chronic inflammatory skin disease fig. 1, which is most common in childhood. Being an important medical and social problem, AD is characterized by a very early manifestation, extensive skin lesions, accompanied by intense itching. Often with AD, secondary infection of the skin with various bacteria and fungi occurs, which is an additional aggravating factor in the patient's condition. In some cases, AD can be the cause of the development of bronchial asthma [1-4].

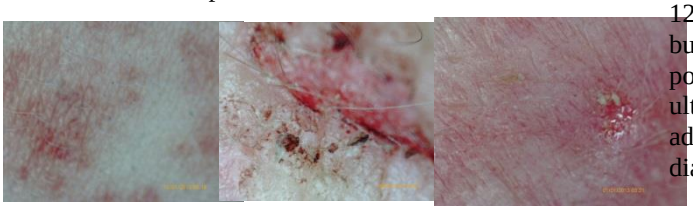

Fig. 1. External manifestations of atopic dermatitis

When objectifying the condition of a patient with AD, instrumental methods for studying the external manifestations of the disease play an important role. Currently, in assessing skin lesions caused by AD, one of the most informative is the dermatoscopy method. Visual analysis of the medical image obtained by dermatoscopy allows the doctor to make a preliminary conclusion about the state of the skin during a specific period of the disease.

The modern dermatoscope market is represented by a wide selection of samples that differ in their functionality and price range.

The VEOS DS3 dermatoscope is a portable digital dermatoscope with a touch-sensitive display, an improved lighting system that allows skin, subcutaneous structures and vascular pattern studies. Dermatoscopy can be performed by contact and non-contact methods (non-polarization and polarization methods). You can adjust the focus in both manual and automatic modes. The design features of the optical system make it possible to avoid optical aberrations, as well as to conduct high-quality focusing and scaling. The device is equipped with 2 contact boards (immersion and cross-polarized).

Dermatoscope (trichoscope) irefly DE330T has an optical increase to 165x; digital up to 495x. Allows you to take pictures with a maximum resolution of 2 mPs (1600 x 1200). Equipped with three-layer glass - 650 nm. and a built-in polarizer with 12 gradations. Video recording is possible. Illumination is represented by a system of 8 ultra-bright LEDs with the possibility of brightness adjustment. The device has dimensions of 13x3.6 cm. The diameter of the chamber is 4 cm.

The DELTA 20 dermatoscope has a chrominance coefficient PRI > 87. the color transmission system is represented by 4 LEDs. Two LEDs can be turned off for side lighting. The optics of the device allows you to make 10-16 times the increase; undistorted over the entire plane. The adjustable eyepiece has individual focus with a correction range from -6 to + 6 dpt.

The Eurolight D30 dermatoscope has a contact glass with a diameter of 25 mm, a lighting system with a lighting intensity (12,000 Lux) with a service life of up to 50,000 hours, a focusing range: from -6 to + 3.5 D, ten times optical magnification, a scale for early detection of pigmentation changes in the skin [5 – 9].

As a recording device during the examination of patients, a video thermoscope UM039 fig. 2 was chosen, having the following characteristics: the possibility of optical magnification up to 200 times, the resolution of the sensing matrix 5 mPs (2880 × 1800 pixels). The device is

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equipped with a built-in adjustable LED lighting unit, a tripod and a 3-inch rotary display.

Fig. 2. Digital video dermatoscope UM039

The effectiveness of solving problems of monitoring the states of objects with random properties, as a rule, depends on the correct selection of the most informative system of parameters (features) that are sensitive to changes in the characteristics of the object. Any control formally implements a test procedure, the effectiveness of the result of which is determined by reliability - the probability of making a correct decision [10]. This approach is complicated by the fact that with the uncertainty of the properties of the object of study, the task of selecting informative parameters becomes problematic. Especially, if metrological support of information transformations in the structure of the control system is difficult when objectification of the patient's condition with AD is carried out by the attending specialist.

Selection of the optimal (by the criterion of maximum reliability) system of informative signs for assessment of patient's condition with AD is the classical task of statistical synthesis in conditions of a priori uncertainty [11, 12]. Characteristics are ranked by information value by value of control validity index [11], or probability of errors [12]. The features of the processing steps [13, 14] and segmentation [15-17] of medical images also lead to errors in the selection of informative features. Also, the fuzziness of evaluation standards in the analysis of the transition from one stage of the disease to another leads to a decrease in prognostic objectification of the severity of the disease.

The solution to the problem is possible when assessing the possibility of using parametric recognition (discrimination) models using serum immunoglobulin indices and immunogram indices, as well as color characteristics of skin areas based on analysis of dermatoscopic images at different degrees of severity of AD.

The purpose of the work is to study the informativity of immunological indicators and dermatoscopic examination data in order to expand the possibilities of predictive objectification of methods for assessing the condition of patients with AD with varying severity.

Materials and methods

The examination of children with AD was carried out on the basis of the Department of Pediatrics Propedeutics No. 2, KhNMU. All patients and their parents gave voluntary consent to participate in the study.

During the examination, anamnesis was collected and the initial dermatological status of the patients was described. The dynamics of the skin process was assessed on the 3rd, 14th, 17th and 28th day of treatment.

The patients received systemic therapy, which included taking antihistamines. Outwardly, we used basic emollient therapy and anti-inflammatory therapy with corticosteroids. The condition of the patients against the background of the therapy was assessed: as clinical recovery - complete resolution of the skin inflammatory process; significant improvement - reduction of the SCORAD index by 75% compared to the initial data; improvement – a decrease in the SCORAD index by 25-50%; no change - decrease in SCORAD index by less than 25%.

Images were recorded using a UM039 digital video dermatoscope. The images were captured onto a microSD card with subsequent transfer of data to a database on a computer.

Construction of a discrimination model to determine informative features

Consider a linear discrimination model. An informative parameter X used to obtain information about a priori undefined properties of an object of control can be considered as a random variable. The latter, in the case of two states of the object (Θ_0 – norm, Θ_1 – deviation from the norm) is characterized by conditional probability distribution densities

$$X \approx f(\mathrm{X}/\Theta_0) \text{ , if } \Theta \in \Theta_0 ,$$

$$X \approx f(\mathrm{X}/\Theta_1) \text{ , if } \Theta \in \Theta_1 .$$

If $m^{(0)}, m^{(1)}, \delta^{(0)^2}, \delta^{(1)^2}$ are mean and dispersions of value X for conditions $\Theta \in \Theta_0$, and $\Theta \in \Theta_1$ accordingly, then under normal (Gaussian) distributions $f(\mathrm{X}/\Theta_0), \mathrm{f}(\mathrm{X}/\Theta_1)$, the probability of decision error in the form of object states is determined under dispersions $\delta^{(0)^2}, \delta^{(1)^2}$ through the probability integral $\Phi(\delta/2)$ [10]

$$P_{er} = 1 - \Phi(\delta/2), \quad (1)$$

where

$$\delta = \left| \frac{m^{(0)} - m^{(1)}}{\delta} \right|. \quad (2)$$

The mean and standard deviation included in equation (2), respectively, are determined by the formulas below

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$$m = \frac{1}{n}\sum_{i=1}^{n} x_i \,,$$

$$\delta = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(\mathrm{x}_i - \mathrm{m}_i)^2} \,,$$

where n – number of measurements of the studied indicator.

If $\delta^{(0)2} \neq \delta^{(1)2}$, then the boundary for P_{er} can be estimated by the inequality

$$P_{er} \leq 1 - \Phi(\delta / 2) \,. \qquad (3)$$

In multivariable monitoring, when the number of informative parameters $X_1, ..., \mathrm{X}_n$ is more than one ($n \geq 2$) variable δ is described by the equation

$$\delta = \sqrt{\sum_{i=1}^{n}\left(\frac{m_i^{(0)} - m_i^{(1)}}{\delta_i}\right)^2} \,, \qquad (4)$$

where δ_i – standard deviation of the i-th indicator, which is determined by the formula

$$\delta_i = \max(\delta_i^{(0)}, \delta_i^{(1)}) \,. \qquad (5)$$

The square of the value δ from the equation (4)

$$\delta^2 = \sum_{i=1}^{n}\left(\frac{m_i^{(0)} - m_i^{(1)}}{\delta_i}\right)^2 \,. \qquad (6)$$

is called the quadratic normalized Euclidean distance between the controlled states (between the vectors of the state averages Θ_0 и Θ_1) [11, 12].

The control object in this case is a vector-column of measured values

$$\overline{x} = \begin{vmatrix} x_1 \\ x_2 \\ . \\ . \\ x_n \end{vmatrix} \,,$$

with conditional *n*-dimensional normal distribution density.

Expression (6) assumes the mutual independence of the vector components in the linear discrimination model [10-12].

The probability of error is less, the greater is, that is δ, the larger the variance-normalized square of the distance between the mean vectors.

A schematic illustration of the distribution of the measured value at two states $\Theta^{(0)}$ and $\Theta^{(1)}$ of the object under study is given in fig. 3.

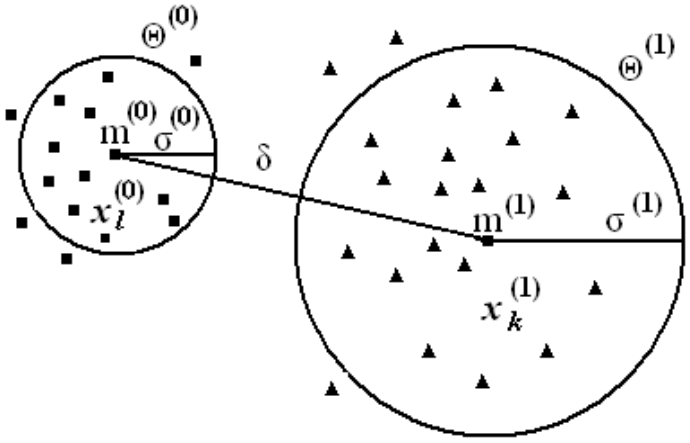

Fig. 3. Schematic illustration of the distribution of the measured value at two states $\Theta^{(0)}$ and $\Theta^{(1)}$ of the object under study

Thus, the variables δ (or δ^2) according to equations (5 and 6) make it possible to quantitatively compare not only single informative diagnostic indicators, but also subsets (systems) of indicators by discriminating ability (in fact, by informativity).

At the same time, for each group of patients the statistical indicators were found: mean values $m_i^{(0)}$ and $m_i^{(1)}$ – standard deviations of the corresponding indicators, and for calculation by formula (5) the maximum standard deviation was chosen according to the formula (6).

In calculations to determine the parameters of prognostic objectification of the assessment of the patient's condition with a severe form of AD, 10 informative parameters $X_i (\mathrm{i} = \overline{1, 10})$ were used, which were displayed in ascending order of numbering:

X_1 – serum immunoglobulin IgE, MOd/ml;

X_2 – serum immunoglobulin IgG, g/l;

X_3 – serum immunoglobulin IgA, g/l%;

X_4 – serum immunoglobulin IgM, g/l;

X_5 – cytotoxic lymphocytes CD8+, %;

X_6 – T-helper lymphocytes CD4+, %;

X_7 – natural killers CD16+, %;

X_8 – Color tone of the skin area H (Hue) in the HSV system;

X_9 – Color saturation of the skin area S (Saturation) in the HSV system;

X_{10} – Color intensity of the skin area V (Volume) in the HSV system.

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For simplicity, in the tables and graphs below, only the number of the informative parameter is indicated.

The first 7 were obtained from laboratory diagnostics data. The last 3 were obtained using dermatoscopy methods.

Patients were divided into two groups - patients with AD in the acute stage and conditional norm (control group).

The results of discriminant analysis when comparing the main indicators of serum immunoglobulins and these immunograms in these groups are given in table. 1. The graphs of the increase in the corresponding normalized Euclidean distance when adding parameters to the discrimination model and the change in the probability of an error in making a prognostic decision when controlling AD in the acute stage with the norm are shown in fig. 4-5, respectively.

Table 1. *Comparison (control) of the effect of serum immunoglobulin indices and immunogram indices in the conditional norm and acute stage of AD*

Method type	**Conditional norm**		**Atopic dermatitis, acute stage**		**Normalized Euclidean distance**	**Normalized Euclidean distance with accumulation**
Indicator / Parameter	m	δ_m	m	δ_m	δ	δ_Σ
1. IgE, MOd / ml	65,2	27,3	201,61	73,31	1,86	1,86
2. IgG, g/l	13,60	7,86	4,44	2,35	1,17	2,19
3. IgA,g/l	1,90	1,25	0,74	0,37	0,93	2,39
4. IgM, g/l	1,45	0,96	0,81	0,45	0,65	2,47
5. CD8+, %	23,40	4,01	20,20	3,76	0,80	2,59
6. CD4+, %	39,01	5,03	38,26	3,61	0,15	2,60
7. CD16+, %	14,41	5,98	13,98	2,42	0,07	2,60
$P_\Sigma error$	0,19					

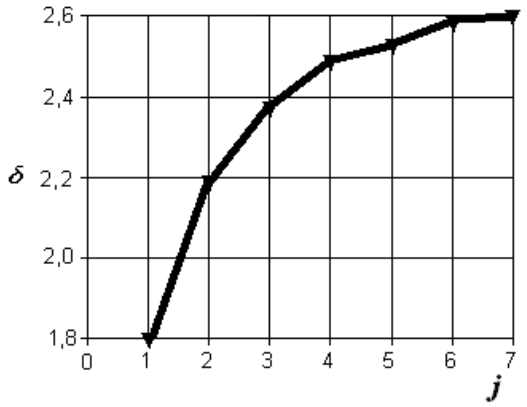

Fig. 4. A graph of the increase in the normalized Euclidean distance when adding parameters (indicators of serum immunoglobulins and immunogram data) to the discrimination model $\delta = F(j)$ when controlling AD in the acute stage and at a conditional norm ($j = 7$ is the dimension of the space of informative parameters)

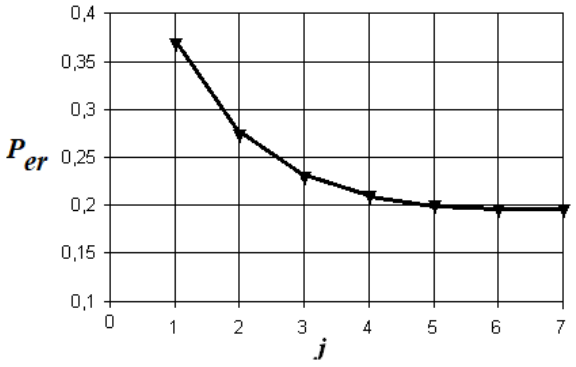

Fig. 5. A graph of the decrease in the error of making a prognostic decision when adding parameters (indicators of serum immunoglobulins and immunogram data) to the discrimination model $P_{er} = f(j)$ when controlling AD in the acute stage and at a conditional norm ($j = 7$ is the dimension of the space of informative parameters)

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It can be seen from these graphs that the greatest contribution to the increase in the normalized Euclidean distance and, accordingly, to the decrease in the probability of error is made by the parameters of immunoglobulin in the blood serum (ranked in descending order of influence), the parameters of the immunogram (except, possibly, CD8 +) practically do not reduce the probability of an error in the assessment the patient's condition and they can be ignored. The total control error when taking into account data only on indicators of serum immunoglobulins and immunograms is 0.19.

If, in addition to the immunological parameters in the discrimination model, take into account the data of digital video dermatoscopy (color characteristics of the skin in the HSV system) (the results are given in table 2), then according to the graphs in fig. 5-6, it can be seen that the greatest contribution to the assessment of the patient's condition is made by a change in the color tone of the skin (reducing the error probability to 0.09) and then changing the saturation (reducing the error probability to 0.07).

Table 2. *Comparison (control) of the total effect of serum immunoglobulin indices and immunogram indices, as well as the color characteristics of skin areas in the conditional norm and in the acute stage of AD*

Method type	**Conditional norm**		**Atopic dermatitis, acute stage**		**Normalized Euclidean distance**	**Normalized Euclidean distance with accumulation**
Indicator / Parameter	m	δ_m	m	δ_m	δ	δ_Σ
ImΣ,					2,60	2,60
H	18°	10,52°	355°	7,26°	2,17	3,38
S	50,14	8,43	40,11	6,95	1,19	3,59
V	98,52	9,30	93,49	8,93	0,54	3,63
$P_\Sigma error$	0,07					

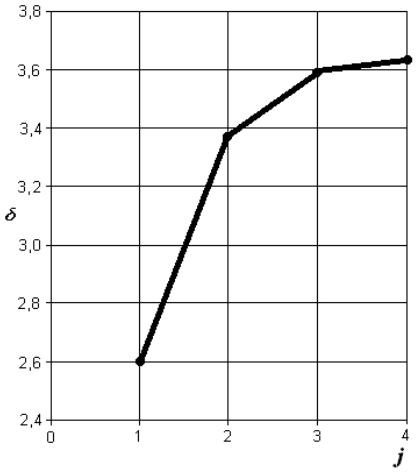

Fig. 6. The graph of the increase in the normalized Euclidean distance when adding parameters (indicators of serum immunoglobulins and immunogram data) and data from digital skin dermatoscopy in the HSV system into the discrimination model $\delta = F(j)$ for AD control in the acute stage and conditional norm ($j = 4$ is the dimension of the space of informative parameters, the first parameter takes into account the integral contribution of immunological data)

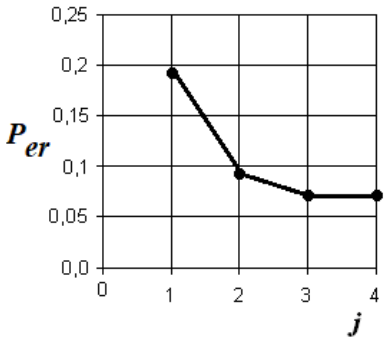

Fig. 7. A graph of the decrease in the error of making a prognostic decision when adding parameters (indicators of serum immunoglobulins and immunogram data) and data from digital skin dermatoscopy in the HSV system into the discrimination model $P_{er} = f(j)$ for AD control in the acute stage with the norm ($j = 4$ is the dimension of the space of informative parameters, the first parameter takes into account the integral contribution of immunological data)

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Analysis of the color characteristics of the skin in the HSV table 2, which are separately shown in table 3-4, demonstrates the possibility of using the digital dermatoscopy method for predictive rapid assessment of the condition of patients with AD. So, in fig. 8–9 show an increase in the normalized Euclidean distance and a change in the probability of a decision-making error by the attending specialist when comparing different pathologies with the norm.

Table 3. *Comparison (control) of the influence of indices of color characteristics of skin areas in normal and acute stages of AD*

Method type	**Conditional norm**		**Atopic dermatitis, acute stage**		**Normalized Euclidean distance**	**Normalized Euclidean distance with accumulation**
Indicator / Parameter	m	δ_m	m	δ_m	δ	δ_Σ
H	18°	10,52°	355°	7,26°	2,17	2,17
S	50,14	8,43	40,11	6,95	1,19	2,47
V	98,52	9,30	93,49	8,93	0,54	2,54
$P_\Sigma error$	0,2					

Table 4. *Comparison (control) of the effect of serum immunoglobulin indices and immunogram indices in normal and acute stages in AD*

Method type	**Conditional norm**		**Atopic dermatitis, acute stage**		**Normalized Euclidean distance**	**Normalized Euclidean distance with accumulation**
Indicator / Parameter	m	δ_m	m	δ_m	δ	δ_Σ
1. IgE, Mod/ml	65,2	27,3	201,61	73,31	1,86	1,86
2. IgG, g/l	13,60	7,86	4,44	2,35	1,17	2,19
3. IgA, g/l	1,90	1,25	0,74	0,37	0,93	2,39
4. IgM, g/l	1,45	0,96	0,81	0,45	0,65	2,47
5. CD8+, %	23,40	4,01	20,20	3,76	0,80	2,59
6. CD4+, %	39,01	5,03	38,26	3,61	0,15	2,60
7. CD16+, %	14,41	5,98	13,98	2,42	0,07	2,60
8. H	18°	10,52°	355°	7,26°	2,17	3,38
9. S	50,14	8,43	40,11	6,95	1,19	3,59
10. V	98,52	9,30	93,49	8,93	0,54	3,63
$P_\Sigma error$	0,07					

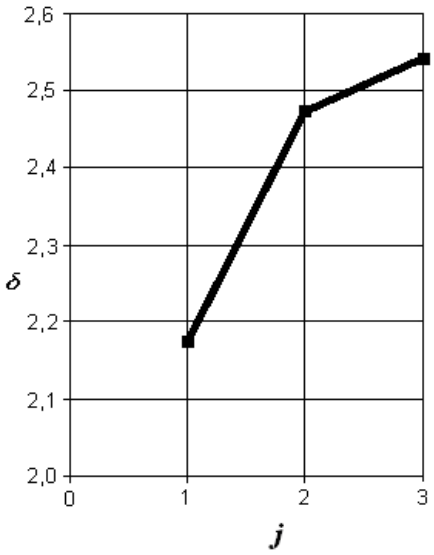

Fig. 8. A graph of the increase in the normalized Euclidean distance when adding color characteristics of the skin in the HSV system to the discrimination model $\delta = F(j)$ when comparing AD in the acute stage with the conditional norm ($j = 3$ is the dimension of the space of informative parameters)

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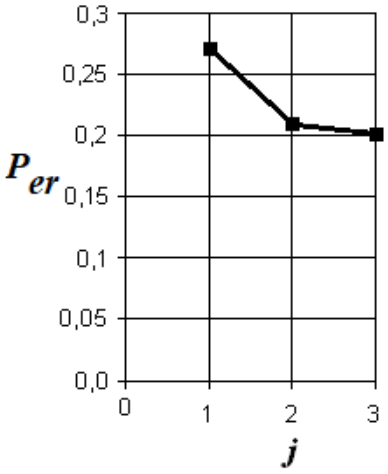

Fig. 9. A graph of the decrease in the error of making a prognostic decision when adding color characteristics of the skin in the HSV system to the discrimination model $P_{er} = f(j)$ when comparing a patient with AD in the acute stage with a conditional norm ($j = 3$ is the dimension of the space of informative parameters)

From the analysis of the graphs in fig. 8 and 9, it is obvious that when comparing AD in the acute stage with the norm, the most significant indicators of immunoglobulin in blood serum (the first 4, ranked in descending order of contribution to the discrimination model) and the indicator of the CD8 + immunogram. The rest of the immunological parameters do not make significant changes in the discrimination model and can be ignored. The total probability of a decision error is 0.19.

Conclusions

Analysis of the color characteristics of the skin in the HSV system showed that when immunological blood parameters are added to the discrimination model, the probability of an error in making prognostic decisions by the attending specialist significantly decreases from 0.19 to 0.07.

Predictive assessment of the condition of a patient with AD only by the color characteristics of the skin in the HSV system makes it possible to control this pathology with an error probability of 0.2. This allows using the digital dermatoscopy method independently for express objectification of the condition of an AD patient without waiting for the data of immunological analyzes.

When a new patient appears, the above indicators are calculated for him and the normalized Euclidean distances to the center of the clusters corresponding to the studied pathologies are calculated. The smallest distance to the center of one of the clusters will correspond to the most probable state of control (norm, or pathology). Also, these distances can be ranked and the probabilities of the correspondence of the given case to specific pathologies can be determined.

The prospect of the work is to substantiate the metrological characteristics of the method to eliminate possible systematic errors associated with the method of obtaining optical information.

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МЕТОД ПРОГНОСТИЧНОЇ ОЦІНКИ СТАНУ ХВОРИХ НА АТОПІЧНИЙ ДЕРМАТИТ НА РІЗНИХ СТАДІЯХ ЗАХВОРЮВАННЯ

Предметом дослідження є розробка методу прогностичної оцінки стану хворих на атопічний дерматит на різних стадіях захворювання. **Метою** роботи є дослідження інформативності імунологічних показників і даних дематоскопічскіх обстежень з метою розширення можливостей прогностичної об'єктивізації методів оцінки стану хворих на атопічний дерматит з різним ступенем тяжкості захворювання. До **завдань** дослідження входить об'єктивізація розмитості еталонів оцінки при аналізі переходу від однієї стадії захворювання до іншої. В якості **методу** рішення поставленої проблеми можливе використання моделей параметричного розпізнавання (дискримінації) з використанням показників імуноглобулінів в сироватці крові і показників іммунограмм, а також колірних характеристик ділянок шкіри на основі аналізу дерматоскопічних зображень при оцінці можливості виникнення різних стадій тяжкості захворювання. До **результатів** дослідження можна віднести те, що в ході дослідження аналіз колірних характеристик шкіри показав, що при додаванні в модель дискримінації імунологічних показників крові ймовірність помилки в прийнятті прогностичних рішень істотно зменшується. Прогностична оцінка стану хворого на атопічний дерматит тільки за кольоровими характеристиками шкіри дозволяє здійснювати контроль даної патології з більш високою часткою ймовірності, що дозволяє використовувати метод цифрової дерматоскопія самостійно для експрес об'єктивізації стану хворого на атопічний дерматит не чекаючи даних імунологічних аналізів. При появі нового пацієнта під час обстежень в умовах стаціонару для нього розраховуються наведені вище показники і обчислюються нормовані евклідовой відстані до центру кластерів, відповідних досліджуваним патологіям. Розраховані відстані можна ранжувати і визначати ймовірності відповідності наведеного випадку конкретним патологіям**. Висновки.** Перспективою подальшої роботи є обгрунтування метрологічних характеристик методу для виключення можливих систематичних похибок, пов'язаних з методом отримання оптичної інформації.

Ключові слова: атопия; дерматит; канал яскравості; дерматоскопія; модель дискримінації.

МЕТОД ПРОГНОСТИЧЕСКОЙ ОЦЕНКИ СОСТОЯНИЯ БОЛЬНЫХ АТОПИЧЕСКИМ ДЕРМАТИТОМ НА РАЗНЫХ СТАДИЯХ ЗАБОЛЕВАНИЯ

Предметом исследования является разработка метода прогностической оценки состояния больных с атопическим дерматитом на разных стадиях заболевания. **Целью** работы является исследование информативности иммунологических показателей и данных дематоскопичских обследований с целью расширения возможностей прогностической объективизации методов оценки состояния больных атопическим дерматитом с различной степенью тяжести заболевания. В **задачи** исследования входит объективизация размытости эталонов оценки при анализе перехода от одной стадии заболевания к другой. **Методы.** Решение поставленной проблемы возможно при оценке возможности использования моделей параметрического распознавания (дискриминации) с использованием показателей иммуноглобулинов в сыворотке крови и показателей иммунограмм, а также цветовых характеристик участков кожи на основе анализа дерматоскопических изображений при различных степенях тяжести заболевания. **Результат.** В ходе исследования анализ цветовых характеристик кожи показал, что при добавлении в модель дискриминации иммунологических показателей крови вероятность ошибки в принятии прогностических решений существенно уменьшается. Прогностическая оценка состояния больного с атопическим дерматитом только по цветовым характеристикам кожи позволяет осуществлять контроль данной патологии с более высокой долей вероятности, что позволяет использовать метод цифровой дерматоскопии самостоятельно для экспресс объективизации состояния больного атопическим дерматитом не дожидаясь данных иммунологических анализов. При появлении нового пациента для него рассчитываются приведенные выше показатели и вычисляются нормированные Эвклидовы расстояния до центра кластеров, соответствующих изучаемым патологиям. Рассчитанные расстояния можно ранжировать и определять вероятности соответствия приведенного случая конкретным патологиям. **Выводы.** Перспективой дальнейшей работы является обоснование метрологических характеристик метода для исключения возможных систематических погрешностей, связанных с методом получения оптической информации.

Ключевые слова: атопия; дерматит; канал яркости; дерматоскопия; модель дискриминации.

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