IJPSR (2022), Volume 13, Issue 1 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 14 March 2021; received in revised form, 21 May 2021; accepted, 02 June 2021; published 01 January 2022

APPLICATION OF THE INFORMATION TECHNOLOGIES IN EARLY PREDICTING THE SEVERITY OF ATOPIC DERMATITIS IN CHILDREN

N. N. Hajiyeva [*1] and İ. A. Gafarov [2]

Azerbaijan Medical University [1], Department II of Children's Diseases, Baku, Azerbaijan
Azerbaijan Medical University [2], Department of Medical Physics and Informatics, Baku, Azerbaijan

Keywords:

Atopic dermatitis, Allergy, Prognosis, Children diseases, Information technologies, Fuzzy logic

Correspondence to Author:
N. N. Hajiyeva

Azerbaijan Medical University, Department II of Children's Diseases, Baku, Azerbaijan.

E-mail: nurangizhaciyeva@gmail.com

ABSTRACT: The application of mathematically based prognostic software is a rational and promising approach to determining disease prognoses. In our research, we identified indicators as prognostic criteria for the development of atopic dermatitis (AD). Our research involved 260 healthy children and 268 newborns with AD. To select the risk factors for predicting the formation of AD, initially, variation and discriminant analyses were used to identify 50 indicators (out of 109 clinical laboratory indicators) that differed statistically. Then, 28 indicators with a high impact on the final result were selected via disbursement analysis; subsequently, 19 indicators based on specificity and sensitivity were fixed. In the next step, via correlation analysis, we focused on 15 antenatal, intranatal, neonatal, and laboratory risk factors that did not correlate with each other. Based on these indicators, software for the prediction of atopic dermatitis was developed. The software-based on MS EXCEL was developed with the application of theories of probability and "fuzzy logic", and the Sp and Sn of the test were evaluated accordingly at 78.5±2.5% and 73.1±2.7%, after verification based on a real situation. Based on the research results, cesarean section, wheezing, conjunctivitis, rhinitis, lactose intolerance, sensitive skin, trouble sleeping, constipation, and levels of CD31, MUC-2 and ITF were found to highly influence the development of atopic dermatitis. Thus, our software is applicable for the assessment of AD development based on the abovementioned factors.

INTRODUCTION: The prognosis of any pathological process in advance is of great importance from both medical and economic points of view. Much attention is paid to diseases due to the deterioration of the body's resources; however, a physician should have maximum information about the near and far future of a patient. Knowledge of individual cases, including assessing the results of various treatment methods, allows classification of patients into high- or low-risk groups and the selection of necessary treatment tactics. The analysis of relevant publications shows that the assessment of disease prognosis based on individual or isolated indicators is not promising. In this context, the preparation of mathematically based prognostic software is a rational and promising approach for prognostication [1-2].

Currently, any event in clinical medicine may be evaluated as a probable process and studied with probability theory methods. These conditions may have positive results for the prognosis of the course of an illness and may allow the application of mathematical methods based on the theory of probability. Great attention has recently been paid to the application of exact sciences in medicine, to

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.13(1).359-68

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.13(1).359-68

the intellectualization of doctoral decisions by developing mathematical expert systems with the help of computers, and to both the prevention of unpleasant results and the mitigation of individual preventive measures [3].

MATERIALS AND METHODS: This research conformed to the requirements of the Science and Technology of the National Committee of Azerbaijan on Bioethics and Ethics. The clinical and laboratory examination of newborns was carried out at the Republican Perinatal Center and Educational-Surgical Clinic of Azerbaijan Medical University between 2015 and 2019. Primary indicators determined to be acceptable prognostic criteria in the development of AD were studied in children involved in the research.

A total of 528 newborns with a gestational age of 36-42 weeks were included in this study, of which 268 had AD. The influence of antenatal, intranatal, and postnatal clinical and laboratory indicators on the development of AD was studied. In addition to a routine peripheral blood sample obtained on the newborns' 1^{st} – 3^{rd} day of life, markers of the immune system, namely, H4R (histamine receptor), PECAM 1 or CD31 (platelet endothelial cell adhesion molecule), MUC-2 (musin-2), a marker of mucous membranes and ITF (intestinal trefoil factor) levels, were identified *via* the Stat Fax immunoenzymometric method of BioSource International Inc. Serum total IgE levels in the blood of infants were determined by a Pharmacia CAP system (Pharmacia & Upjohn Diagnostics AB, Uppsala, Sweden). According to the classification approved in Great Britain, AD diagnosis in children was identified on the basis of 3 criteria (characteristic localization of skin damage, presence of atopy in anamnesis, skin dryness) alongside itching. The SCORAD (Scoring Atopic Dermatitis) scale approved by European dermatovenerologists was used to evaluate the severity of AD. All indicators in the course of the research were calculated via variation (H-Kruskal-Wallis), discriminant (Pearson chi-square), dispersion (ANOVA test – F-Fisher), correlation (ρ-Spearman), and ROC analyses and proven methods of biostatistics medicine. A discriminant analysis algorithm was used to resolve the diagnostic issues. At this stage, 50 prognostic criteria were selected for further analyses.

Correct application of probability methods requires correlative no dependence of prognostic criteria. Thus, overlapping of unilateral results of correlative indicators could lead to a strong disruption of a true prognosis. The calculation of the rate of spread of every indicator and its change allows assessment of only one clinical prognostic criterion; however, these indicators occur altogether in many cases, and thus, it is impossible to determine the level of their significance on individual cases with traditional assessment methods. Mathematical processing and quantitative evaluation of the abovementioned indicators could allow determining the power of influence of the indicators in advance on all possible joint cases. These challenges emphasize the need for mathematical approach in the resolution of these issues.

Blood Collection: Venous blood was collected in ethylenediaminetetraacetic acid (EDTA)-containing tubes on days 1–3 and 7–10 and centrifuged for 15 min. The samples were stored in aliquots at -70 °C until analysis. No venous punctures were performed for the sole purpose of study-related analysis.

Measurement of Serum MUC-2, ITF, CD31 and H4R Concentrations in Peripheral Blood: The plasma concentrations of MUC-2, ITF (Life Science, Wuhan, China), CD31, and H4R (Cayman Chemical Company, Ann Arbor, MI, USA) were measured using commercial enzyme-linked immune-sorbent assay (ELISA) kits based on a standard enzyme.

Immunoassay Procedures: The specimens were diluted according to the manufacturer's instructions for the ELISA kits to obtain the optimal density. The expression levels of MUC-2 and ITF are reported in ng/mL, whereas those of IgG1, CD31 and H4R are reported in pg/mL.

Results: Initially, out of 109 clinical and laboratory indicators affecting children in the perinatal period, 50 indicators were identified by the discriminant (Pearson chi-square) and dispersed (ANOVA test - F-Fisher) methods, which were later refined by the H-Kruskal-Wallis criterion. Clinical signs predominated among the risk factors. According to statistical calculations, 52.2% of the group II children had allergic conjunctivitis ($pH<0.001$),

13.4% had toxic erythema (pH=0.005), 66.0% had wheezing breathing (pH<0.001), 63.8% had sensitive skin (pH<0.001), 64.6% had trouble sleeping (pH=0.039), and 3.4% had vomiting (pH=0.012); these factors were significantly more frequent in the group II versus the group I children.

However, no statistically significant difference was found between the groups for diaper dermatitis (pH=0.075) and regurgitation (pH=0.425). Among these symptoms, bloating (pH=0.001) was more common in the group I children (chart 1). Among the perinatal risk factors for AD development, laboratory studies revealed that CD31, MUC-2 and ITF levels were significantly higher in group II children (p<0.001) **Table 1**.

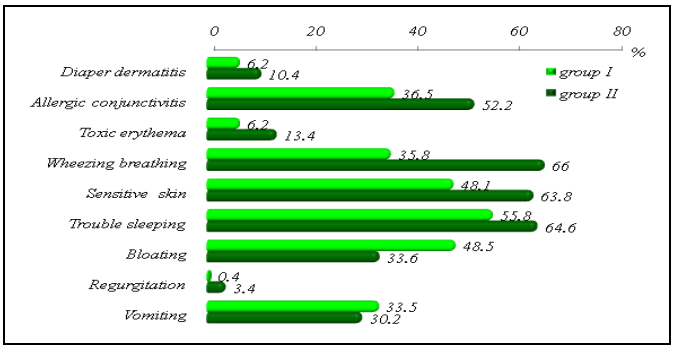

CHART 1: FREQUENCY OF CLINICAL SIGNS IN NEWBORNS

TABLE 1: THE ROLE OF LABORATORY INDICATORS IN THE DEVELOPMENT OF AD

Factor	Groups	n	M	±m	min	max	P_F	P_H
CD 31, mq/l	AD-	44	18.6	4.0	0.51	131.97	0.013	0.001
	AD+	54	36.3	5.4	0.23	181		
H4R, mq/l	AD-	49	15.3	2.2	0.23	181	0.140	0.052
	AD+	73	27.2	6.4	0	35.27		
MUC-2, mq/l	AD-	62	14.0	3.5	0.00	101.00	0.001	0.001
	AD+	70	37.7	4.7	0.00	111.00		
ITF, mq/l	AD-	40	11.9	1.2	0.0	28.3	0.001	0.001
	AD+	61	26,5	2.4	0.0	78.0		
IgE, IU/ml	AD-	48	25.9	8.4	1	22.8	0.251	0.572
	AD+	43	43.7	13.3	1.2	418		
Vit. D, ng/ml	AD-	186	22.7	0.8	6	66.5	0.492	0.923
	AD+	159	23.6	1.0	6.8	60		

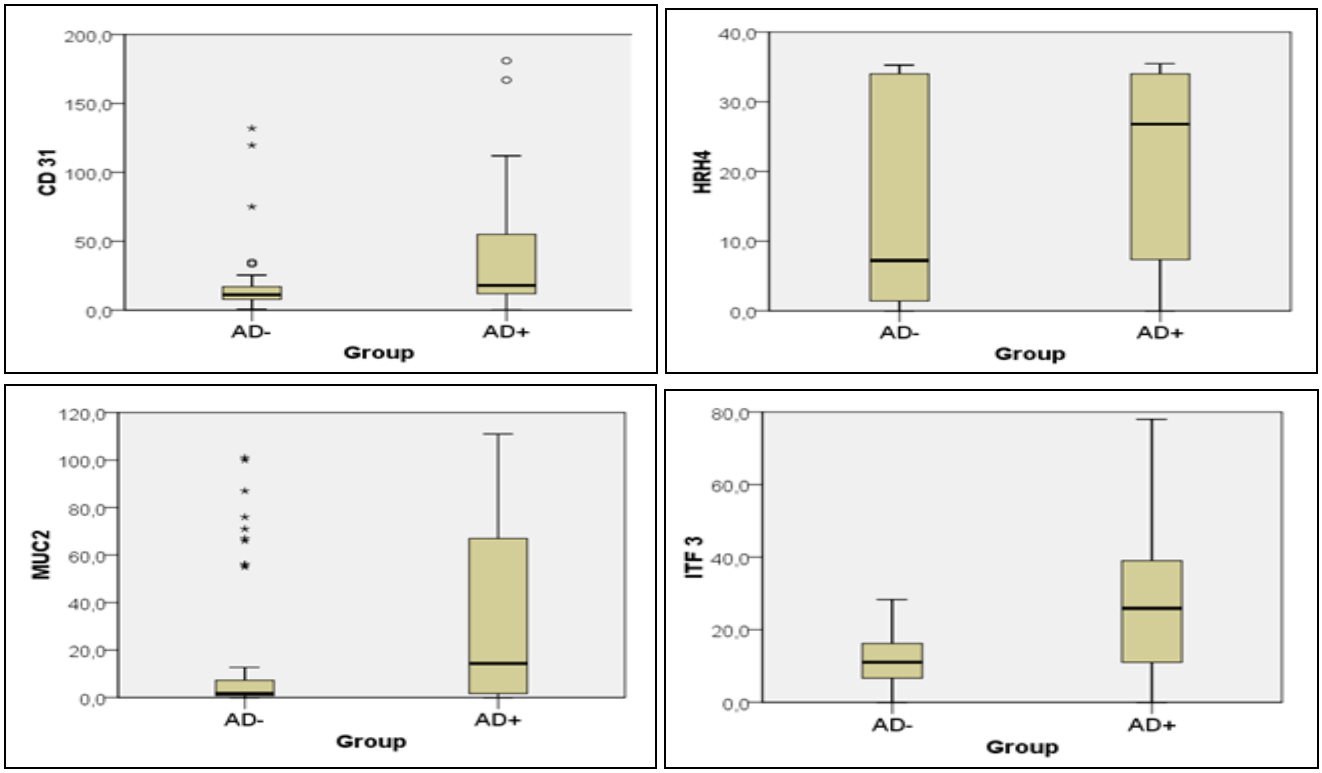

CHART 2: COMPARISON OF THE INTESTINAL BARRIER MARKER LEVELS BY THE METHOD OF VARIATION STATISTICS

In this study, we compared the levels of intestinal barrier markers by the method of variation statistics (chart 2). Higher concentrations of MUC-2 and ITF were found in the first days of the postnatal period in the group of children with subsequent formation of AD. The proven nature of this difference between the groups was established for MUC-2.

Given the exposure of the fetus to multiple sensitizing impacts during the formation of the immune system during the perinatal period, first, the sensitivity (Sn), specificity (Sp), and GDV of statistically valid and different perinatal risk factors were studied **Table 2**.

TABLE 2: INFORMATIVE VALUE OF PERINATAL RISK FACTORS IN THE FORMATION OF AD

Statistical parameter	Risk factors			
	Place of residence	Allergy in parents	Season of birth	Cesarean section
Sensitivity (Sn)	60.1±3.0%	67.9±2.9%	13.8±2.1%	67.5±2.9%
Specificity (Sp)	52.3±3.1%	60.4±3.0%	94.2±1.4%	41.9±3.1%
General diagnostic value (GDV)	56.3±2.2%	64.2±2.1%	53.4±2.2%	54.9±2.2%
Effect of evaluation under positive predictive value (pPV)	56.5±2.9%	63.9±2.8%	71.2±6.3%	54.5±2.7%
Effect of evaluation under negative predictive value (nPV)	56.0±3.2%	64.6±3.1	31.5±2.3%	55.6±3.5%
Likelihood ratio of positive result (LR+)	1.26 unfit	1.71 unfit	2.39 satisfactory	1.16 unfit
Likelihood ratio of negative result (LR-)	0.76 unfit	0.53 unfit	0.91 unfit	0.77 unfit

Among these factors, the highest Sn (67.9±2.9%) and GDV (64.2%) were noted for the allergy in parents factor, while the highest Sp (94.2±1.4%) and the effect of evaluation under positive predictive value (pPV) (71.2±6.3%) and likelihood ratio of a positive result (2.39 – satisfactory) were noted for the season of child's birth factor. The Sp, Sn and GDV of the neonatal risk factors were studied in the course of this research **Table 3**.

TABLE 3: INFORMATIVE VALUE OF NEONATAL RISK FACTORS IN THE FORMATION OF AD

Statistical parameter	Factors						
	Wheezing breathing	Allergic conjunctivitis	Allergic rhinitis	Lactose intolerance	Sensitive skin	Trouble sleeping	Functional constipation
Sn	66.0±2.9%	52.2±3.1%	83.2±2.3%	44.8±3.0%	63.8±2.9%	64.6±2.9%	38.2±2.9%
Sp	64.2±3.0%	63.5±3.0%	53.1±3.1%	78.3±2.8%	51.9±3.1%	44.2±3.1%	76.5±2.6%
GDV	65.2±2.1%	57.8±2.1%	68.4±2.0%	61.4±2.1%	58.0±2.1%	54.5±2.2%	54.4±2.2%
pPV	65.6±2.9%	59.6±3.2%	64.6±2.6%	68.2±3.5%	57.8±2.9%	54.4±2.8%	59.1±4.0%
nPV	64.7±3.0%	56.3±2.9%	75.4±3.2%	58.0±2.6%	58.2±3.2%	54.8±3.4%	55.2±2.6%
LR+	1.26 unfit	1.43 unfit	1.77 satisfactory	2.08 satisfactory	1.31 unfit	1.16 unfit	1.40 unfit
LR-	0.76 unfit	0.75 unfit	0.33 unfit	0.70 unfit	0.70 unfit	0.80 unfit	0.88 unfit

The highest Sn and GDV among the abovementioned factors was for allergic rhinitis; the highest Sp was for lactose intolerance and functional constipation; the highest (pPV) was for lactose intolerance and wheezing and the highest effect of evaluation under negative predictive value was for allergic rhinitis.

The likelihood ratio of positive results (LR+) was noted in the frequency of symptoms of allergic rhinitis (1.77 – satisfactory) and lactose intolerance (2.08 – satisfactory). The symptoms in question are of great importance in the prognosis of AD.

In the second stage, via disbursement analysis, we came to 28 indicators that have a high impact on the final result.

ROC analysis was conducted for the evaluation of laboratory indicators (prognostic markers), cutoff points were determined on the basis of coordinates of ROC curves and the Sn and Sp of the markers were calculated.

A sensitive ROC test was based on laboratory indicators noted between statistically valid differences (chart 3).

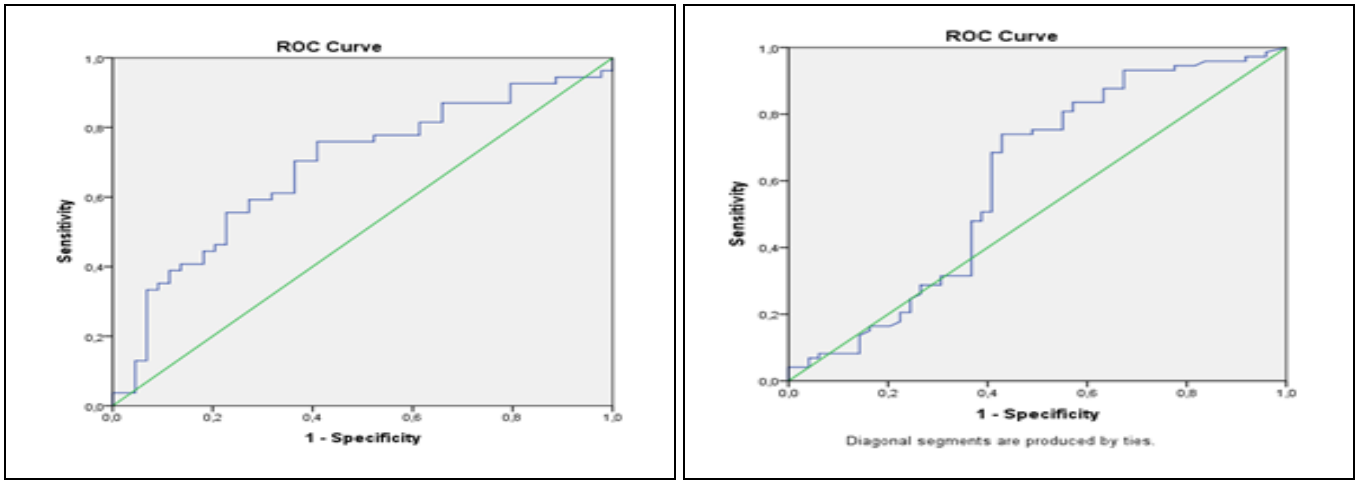

CHART 3: RESULTS OF ROC ANALYSES OF THE CD31 AND H4R MARKERS

Volatility of test result(s)	Area	Standard error	Asymptotic sig.	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
CD31	0.85	0.054	0.002	0.578	0.791
H4R	0.604	0.056	0.052	0.494	0.714

Apparently, a large part of the ROC curve for the cytokine CD-31 marker, which reflects immunological changes, is located above the standing line and the area of the Sp of H4R (genetic allergic marker) in the reliability interval at 95% comprises 0.604±0.56 (p=0.52). ROC analysis was conducted on the mucous markers MUC-2 and ITF of the endothelial barrier, which are seen as more sensitive in AD prognosis (chart 4).

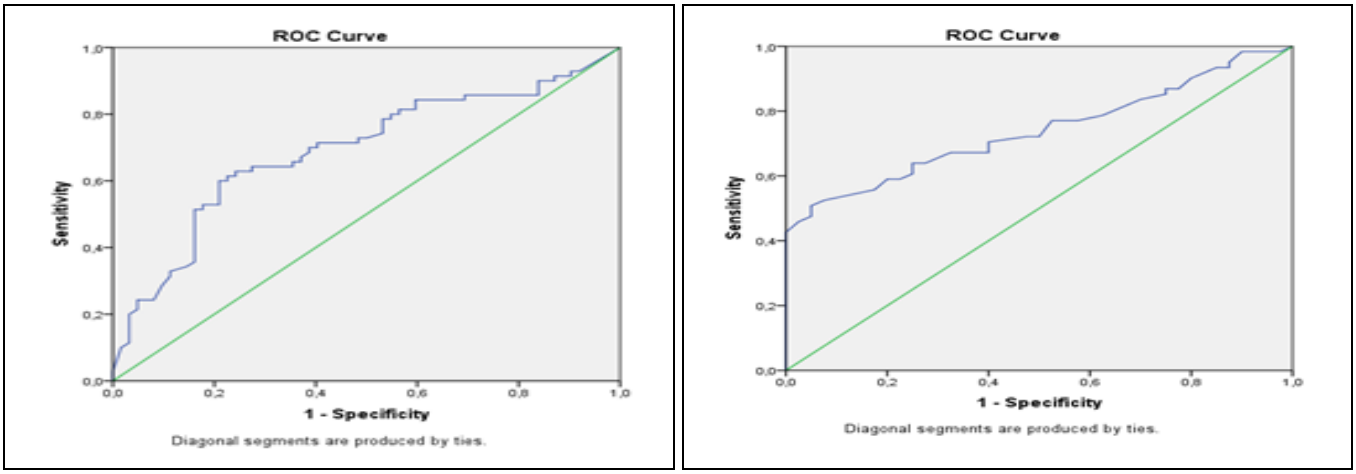

CHART 4: RESULTS OF ROC ANALYSES OF MUC-2 AND ITF

Volatility of test result(s)	Area	Standard error	Asymptotic sig.	Asymptotic 95% confidence interval	
				Lower bound	Upper limit
MUC-2	0.692	0.046	< 0.001	0.601	0.783
ITF	0.740	0.048	< 0.001	0.645	0.834

According to the ROC curves, MUC-2 and ITF mucous membrane markers have a high Sp and informative nature in children with AD.

Thus, the area of the Sp of MUC-2 calculated under the ROC curve equals 0.692±0.046 (p<0.001), and referential indicators in the reliability interval of ITF at 95% vary between 0.645 and 0.834 (p<0.001). The next stage aimed to identify cutoff points – the farthest point from the standing line among interval figures at a variation interval of the indicators in the ROC analysis result.

The calculation was conducted on statistically valid differing indicators based on ROC analysis **Table 4**.

TABLE 4: ROLE OF MOLECULAR MARKERS IN THE FORMATION OF AD

Statitical parameter	Indicators			
	CD-31	H4R	MUC-2	ITF
Cutoff	11.8	2.3	8.0	25
Sn	75.9±5.8%	83.6±4.3%	60.0±5.9%	50.8±6.4%
Sp	59.1±7.4%	42.9±7.1%	79.0±5.2%	95.0±3.4%
GDV	68.4±4.7%	67.2±4.3%	68.9±4.0%	68.3±4.6%
pPV	69.5±6.0%	68.5±4.9%	76.4±5.7%	93.9±4.2%
nPV	66.7±7.5%	63.6±8.4	63.6±5.5%	55.9±6.0%
LR+	1.86 unfit	1.46 Unfit	2.86 satisfactory	10.16 excellent
LR-	0.41 satisfactory	0.38 satisfactory	0.51 unfit	0.52 unfit

Based on the factors studied, ITF, which is synthesized by goblet cells of the mucous membranes, has the highest informative value, and the quantity of this factor (n=101 persons) is higher than 25.0; its Sp, informative value, and GDV were 50.8±6.4%, 95.0±3.4%, and 68.3±4.6%, respectively. The effect of evaluation under positive and negative predictive values was 93.9±4.2 and 55.9±6.0, respectively, proving the great importance of this indicator in AD prognosis.

According to the table, (LR+) ITF was evaluated as excellent, and CD-31 and MUC-2 were assessed as satisfactory; (LR-) CD-31, H4R, and MUC-2 were evaluated as satisfactory. Among these markers, the mucosal markers MUC-2 and ITF had the most insightful results, with the highest Sp and Sn.

In the next stage, 19 indicators of practical importance based on specificity and sensitivity were selected (chart 5).

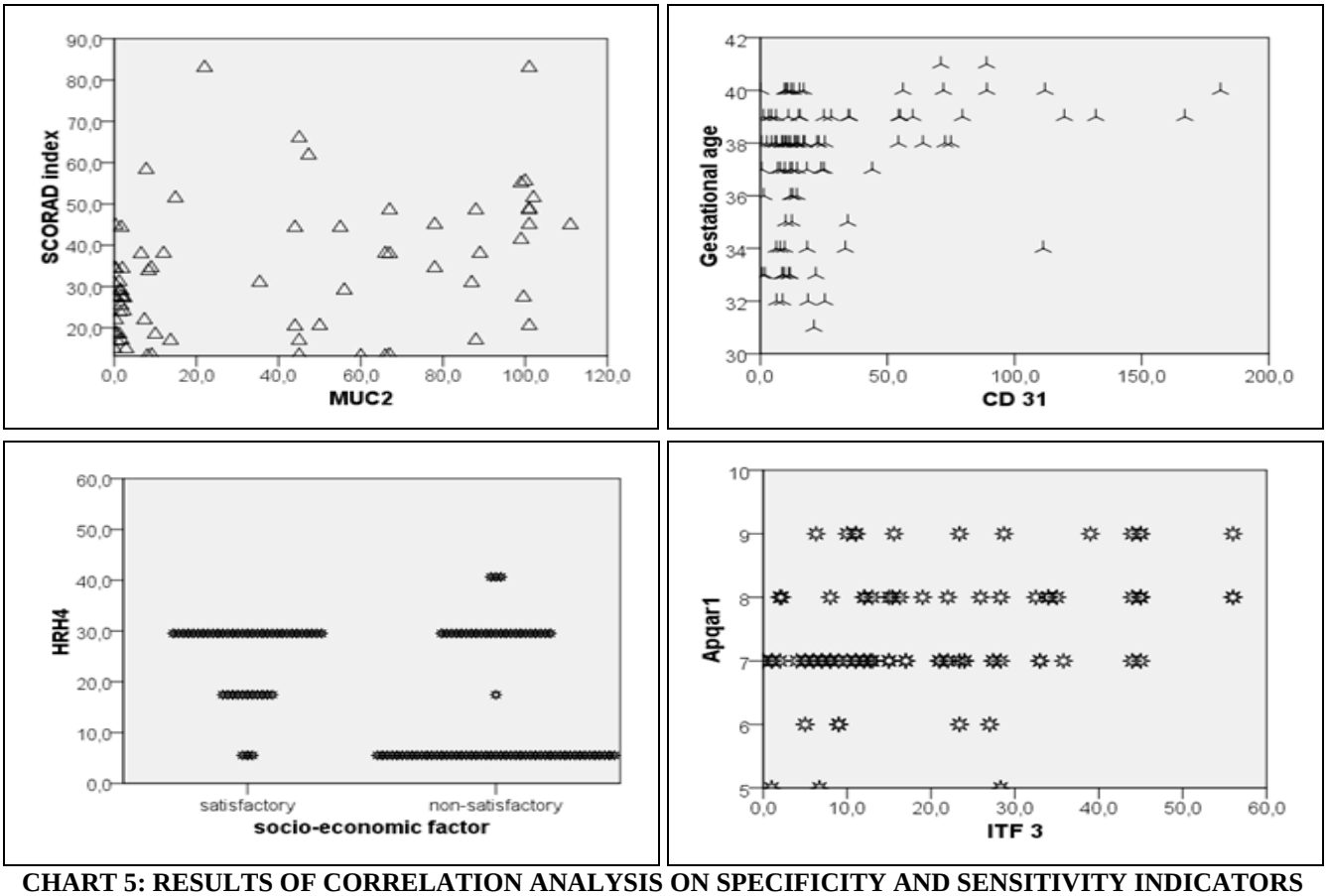

CHART 5: RESULTS OF CORRELATION ANALYSIS ON SPECIFICITY AND SENSITIVITY INDICATORS

According to the results of the study with the level of MUC-2 on the SCORAD scale (ρ=0.380; p=0.001), which determines the severity of AD, a primary correlation was established between an unsatisfactory socioeconomic environment in which the pregnant woman lives, the level of H4R in the child's blood (ρ = –0.341; p < 0.001), the gestational age of the baby CD31 ~ (ρ=0.298; p =

0.003) and the value of the Apgar scale in the 1st minute of life ITF ~ ($\rho = 0.405$; $p < 0.001$). We selected 15 noncorrelative factors for correlation analysis (p-Spearman) of the results. First, we distributed these indicators under the principle of available/not available, *i.e.,* there is AD/there is no AD. In this case, it was advisable to apply the Bayes formula.

The unique "ADYR-2019" software based on the MS EXCEL-2013 component was developed in the visual basic algorithm language for modeling the abovementioned ADYR (abbreviation from the native Azerbaijani name – "Atopik dermatitin yaranma riski") risk of formation of atopic dermatitis findings. The software requires a doctor to enter patient data in necessary boxes within seconds with the help of capabilities at the user level. The software controls the information entered as well; thus, a doctor must carefully mark the box with false data as "False". It should be noted that cases with missing patient information are also taken into account.

In this regard, the result is calculated even in the absence of information in a box. However, the inclusion of all data selected in the program ensures a more accurate result; thus, it is advisable to mark all boxes.

Such information would play a vital role in the selection of future treatment tactics by a physician. The software is protected from accidental amendments and requires standard MS OFFICE software. The software has a capacity of less than 50 Kbyte. It can be found at the URL address: https://www.amu.edu.az/az/cafedra/31/311/1274?cafedra=1277&cafedra_s=5784. The ADYR-2019 software calculates the probability of AD in an examined child. The following factors are included in the ADYR-2019 software: allergy in parents, the season of birth of child, type of delivery, wheezing, allergic conjunctivitis, allergic rhinitis, lactose intolerance, skin sensitivity, trouble sleeping, functional constipation, and CD31, H4R, MUC-2 and ITF blood levels. The result of the program is displayed as a chart (chart 6).

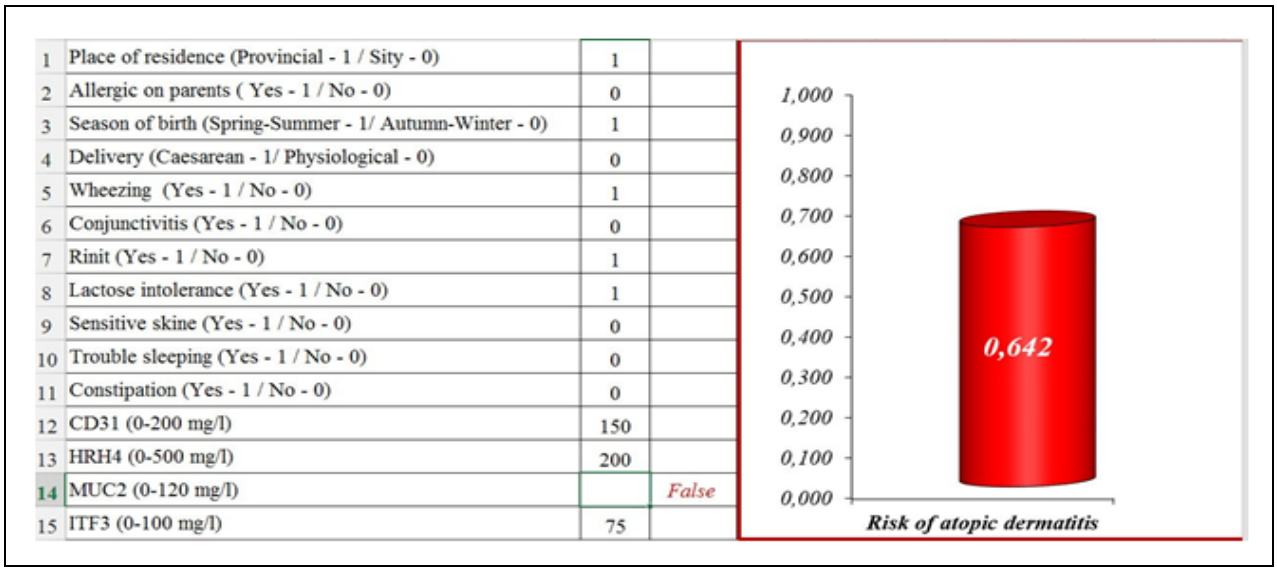

CHART 6: ONE RESULT OF APPLICATION THE ADYR-2019 SOFTWARE

All indicators studied in the groups with and without AD were taken into consideration for the evaluation of the results. According to the quantity of real positive and real negative results, the Sp and Sn were evaluated on the ADYP-2019 software. A cutoff point slightly differing from 0.50 was determined on the basis of the results of the ROC test. This point was equal to 0.52. The results of the indicators were lower than 0.52 in 204 out of 260 cases in the group without AD.

In other words, the Sp of this test was 78.5±2.5%. High results in 196 out of 268 cases (≥0.52) allowed evaluation of the Sn (73.1±2.7%) of the program in the group with AD. The general diagnostic value of the ADYR-2019 program was 75.8±1.9%. The figures for positive predictive value (pPV) and negative predictive value (nPV) of 77.8±2.6% and 73.9±2.6%, respectively, confirm the efficient significance of the applicable forecasting program.

It should be noted that a positive solution direction in forecasting AD in children was not observed in pediatric practice. The power of influence of the factors presented on the model prepared on the basis of the results was calculated via the Fischer-Snedecor method at the next stage, and the final results are described in **Table 5**.

TABLE 5: INFORMATIVE VALUE OF FACTORS INVOLVED IN THE AD PROGNOSIS MODEL IN NEWBORNS

Risk factor	Odds Ratio			Fischer-Snedecor				p
	OR	95% CI		EIF%	95% LB	95% UB	F	
Place of residence	1.65	1.17	2.33	1.6	0.8	2.3	8.4	0.004
Allergy in parents	3.23	2.26	4.61	8.8	8.1	9.4	50.5	<0.001
Season of birth	2.62	1.40	4.89	1.9	1.1	2.6	9.9	0.002
Cesarean section	1.50	1.05	2.14	1.0	0.2	1.7	5.1	0.024
Wheezing breathing	3.49	2.44	5.00	10.1	9.4	10.8	59.1	<0.001
Allergic conjunctivitis	1.90	1.34	2.69	2.6	1.8	3.3	13.8	<0.001
Allergic rhinitis	5.61	3.75	8.38	17.0	16.4	17.6	107.8	<0.001
Lactose intolerance	2.95	2.02	4.32	6.5	5.8	7.2	36.4	<0.001
Sensitive skin	1.90	1.34	2.70	2.6	1.9	3.3	13.9	<0.001
Trouble sleeping	1.44	1.02	2.05	0.8	0.1	1.5	4.3	0.039
Functional constipation	1.59	1.09	2.34	1.1	0.4	1.8	5.8	0.016
CD 31	4.56	1.92	10.83	14.5	11.0	18.0	16.3	<0.001
H4R	3.81	1.65	8.82	9.3	6.3	12.3	12.3	0.001
MUC-2	5.65	2.60	12.29	18.5	16.0	21.0	29.5	<0.001
ITF	19.63	4.35	88.69	29.6	26.8	32.4	41.6	<0.001

Thus, the normal barrier function of the mucous membrane of the intestines reduces the risk of developing inflammatory processes in the digestive system in the 1st month of a child's life. The development of AD due to the abovementioned factors is explained by a disorder of integrity of the mucous membrane barrier. Allergies in parents among antenatal risk factors and wheezing, allergic conjunctivitis, allergic rhinitis, lactose intolerance, sensitive skin, and levels of CD31, H4R, MUC-2, and ITF among neonatal risk factors attained great importance in the development of systemic inflammation of mucous membranes.

DISCUSSION: The aim of this study was to identify prognostic criteria for the development of AD (atopic dermatitis) in children. The atopic history of the parents has been used as an important predictor for childhood atopy [4-6]. Many factors are associated with atopic dermatitis, including allergic conjunctivitis (pH<0.001), toxic erythema (pH=0.005), wheezing breathing (pH<0.001), sensitive skin (pH<0.001), trouble sleeping (pH=0.039) and vomiting (pH=0.012). Although there is a predominance of papers pointing to vitamin D as a protective factor, various studies actually identify it as a risk factor for AD 7. According to the results of this study, the amount of vitamin D and Ig E in the blood of a newborn was not informative for predicting AD.

Thus, identifying the most significant early perinatal risk factors predisposing a newborn to the development of postnatal allergic pathology will make it possible to develop a set of therapeutic and prophylactic measures to prevent the formation of AD. Hyperproduction of intestinal goblet cells from the first days of life reflects the presence of a systemic inflammatory reaction of the mucous membranes, which can be of significant importance in the immunopathogenesis of atopic disease [8].

The presence of a relationship between the level of MUC-2 measured in the first days of life and the risk of AD formation allows us to propose using this marker to monitor and predict the further course of AD. Among the perinatal risk factors for AD development, laboratory studies revealed that the levels of CD31, MUC-2, and ITF were significantly higher in group II children (p<0.001). When analyzing the level of intestinal factors depending on the severity of AD, we found a significantly high level of MUC-2 in severe AD. A similar relationship was found for ITF, but no statistical significance was found. We believe that the increase in MUC-2 expression in the intestinal mucosa has a compensatory character under conditions of damage against the background of perinatal risk factors. Under conditions of perinatal hypoxia, inflammatory processes are accompanied by a characteristic transformation of mucins:

sulfation decreases and sialylation increases. This leads to a decrease in the resistance of mucin to bacterial resolution and increases the permeability of the intestinal mucous barrier [9]. Despite different ratios of Th1 and Th2 allergic heredity in various age groups during the antenatal period of the formation of the atopic phenotype, Th2 cells remain dominant for some time after birth. The increase in Th2 synthesis has an adaptive nature at the end of the prenatal period and protects the afterbirth from potential Th1 toxicity. Thus, the fetus becomes ready for the development of expected atopy within this period; an "open window" phenomenon is noted, *i.e.*, it is prepared for sensitization and manifestation of atopic diseases (AD, allergic rhinitis, and bronchial asthma) 10. The Sp, Sn, and GDV of neonatal risk factors were studied in the course of this research.

The intestinal barrier has recently been determined to be very significant for the pathogenesis of immune processes [11]. The identification of the importance of immune and mucosal markers in the prognosis of AD since the early neonatal period may prevent the development of allergic pathologies appearing in later years. In consideration of the great importance of immunological (CD31 and H4R) and mucous membrane molecular markers (MUC-2 and ITF) in the development of AD, a more sensitive ROC test was performed on laboratory indicators with statistically valid differences.

Allergic rhinitis, lactose intolerance, MUC-2 and ITF factors, among laboratory changes, were of great importance in AD prognosis in newborns due to their high specific and informative value. This research confirmed the involvement of markers of the mucous membrane in the formation of barrier function and the development of atopy. Damage to the intestinal mucosa influenced by perinatal risk factors was an initiating and significant factor of atopic allergy. The identification of early and significant risk factors in the formation of AD would allow the classification of risk groups with postnatal allergic pathology and the preparation of a set of treatment and preventive measures towards the prevention of the formation of AD. Hypersecretion of goblet cells in the form of a high MUC-2 concentration from the first days of life suggests damage to the intestinal mucosal barrier under the influence of perinatal risk factors with AD formation at subsequent stages of ontogenesis. Marked changes in MUC-2 levels compared with ITF indices in AD indicate a greater sensitivity of this component of the intestinal barrier to damaging effects in the antenatal period. In conclusion, MUC-2 indices can be considered biomarkers for predicting AD development in newborns prone to atopy. We selected 15 noncorrelative factors during the correlation analysis (p-Spearman) between the results. According to our study, the direct correlation between the unsatisfactory socio-economic environment of a pregnant woman and the level of H4R in the blood of the child assessed on the SCORAD scale, which determines the severity of AD with the level of MUC-2, and between the level of ITF with the gestational age of the baby CD31 ~ and Apgar scale in 1 min of life was established.

The next stage of the attempt to establish a prognostic program exceeded the borders of the theory of probability and the science of mathematical statistics. Thus, it was impossible to determine a one-digit probability of AD formation on a specific unit of laboratory indicators. Therefore, we had to refer to elements of the theory of "fuzzy" logic. To this end, we gathered the laboratory results of children with and without AD into a "fuzzy" multitude in the form of n-sized ellipsoids, with focuses on medians of AD+ and AD- multitudes. Then, we divided this ellipsoid into a multitude of interconnected ellipsoids through percentile evaluation. This allowed us to determine the point of connection of ellipsoid in a one-digit form (given any set of laboratory results) on every specific occasion. As the focuses of the ellipsoid are obvious, the distances until the focuses of each point became a metric for us. These figures were normalized and recognized as an unconditional probability, which allowed us to conclude calculations on a forecasting model again under the Bayes formula. According to the requirements of "fuzzy logic" theory, we rejected absolute "0" and absolute "1" for determining the distance to avoid any indefinite situations and made use of 0.01 or 0.05 instead of "0" and 0.99 or 0.95 instead of "1" – figures close to former ones, depending on the shape of the ellipse on each specific occasion.

CONCLUSION: A model of AD prognosis was developed by identifying clinical and molecular predictors significant in developing allergies.

According to the AD model, the power of influence of place of residence, allergy in parents, the season of birth, cesarean section, wheezing breathing, allergic conjunctivitis, allergic rhinitis, lactose intolerance, sensitive skin, trouble sleeping, functional constipation, and levels of CD31, MUC-2 and ITF were higher.

Hyperproduction of mucous membranes recorded since the first days of a child's life reflects systemic inflammatory reactions and is of great importance in the immunopathogenesis of AD. The relationship between symptoms evaluated at the early neonatal period and the risk of atopic dermatitis formation was identified to be insightful during the prognosis of the same factors at the perinatal period.

The increase in sensitive markers of the intestinal system at the early neonatal period is explained by their presence in epithelial defense and the fundamental protection of mucous membranes. In addition to changes in the skin, mucosal imbalance in question leads to mucosal inflammation overall. Changes in the mucosal system due to the penetration of various allergens are an immune-pathogenic link of AD and are significant in its development and prognosis.

Because the informative value of all factors present in prognosis is accompanied by statistical validity, the use of all factors is expedient in the model for the purpose of a more precise result.

ACKNOWLEDGEMENT: We would like to acknowledge help of the colleagues from the Republican Perinatal Center in Baku and the Educational-Surgical Clinic of the Azerbaijan Medical University where the clinical and laboratory examination of newborns was carried out between 2015 and 2019.

CONFLICTS OF INTEREST: Authors have no conflicts of interest to disclose with the publication of this manuscript.

REFERENCES:

1. Smolkin YS, Balabolkin II, Gorlanov IA, Kruglova LS, Kudryavtseva AV, Meshkova RY, Migacheva HB, Khakimova RF, Cheburkin AA, Kuropatnikova EA, Lyan NA, Maksimova AV, Masalskiy SS and Smolkina OY: Consensus document APAIR: atopic dermatitis in children — update 2019 (short version) part 1. Allergology and Immunology in Pediatrics 2020; 60(1): 4-25
2. Sahiner UM, Buyuktiryaki B, Gungor HE, Sahiner N, Turasan A, Torun YA and Sekerel BE: Factors that predict disease severity in atopic dermatitis: The role of serum basal tryptase. Allergy Asthma Proc 2018; 39(5): 371-6.
3. Correlation between Personal Hygiene, Household Hygiene, and Atopic Dermatitis in Elementary School Children in Indonesia September 2020. Majalah Kedokteran Bandung 2020; 52(3):144-8.
4. Flohr C and Mann J: New insights into the epidemiology of childhood atopic dermatitis. Allergy 2004; 69(1): 3-16.
5. Takashi F, Shelly ZCL, Yuka N, Seiji K and Oyoshi MK: Influences of maternal factors over offspring allergies and the application for food allergy. Front Immunol 2019. doi.org/10.3389/fimmu.2019.01933
6. Liao SL, Tsai MH, Yao TC, Hua MC, Yeh KW and Chiu CY: Caesarean section is associated with reduced perinatal cytokine response, increased risk of bacterial colonization in the airway, and infantile wheezing. Sci Rep 2017; 7: 9053.
7. Benson AA, Toh JA, Vernon N and Jariwala SP: The role of vitamin D in the immunopathogenesis of allergic skin diseases. Allergy 2012; 67(3): 296-01.
8. Mueller NT, Bakacs E and Combellick J: The infant microbiome development: mom matters. Trends Molecular Medicine 2015; 21(2): 109–17.
9. Gadzhieva NN, Eyubova AA, Panakhova NF and Gafarov IA: Predictor value of molecular markers of intestinal mucous membranes in the development of atopic dermatitis in children. PEDIATRIA 2019; 98(6): 71-8.
10. Paternoster L, Standi M and Waage J: Multi-ethnic genome-wide association study of 21,000 cases and 95,000 controls identifies new risk loci for atopic dermatitis. Nat Genet 2015; 47(12): 1449-56.
11. Chu DM and Prince AL: Maturation of the infant microbiome community structure and function across multiple body sites and in relation to mode of delivery. Nature Medicine 2017; 23(3): 314–26.

How to cite this article:
Hajiyeva NN and Gafarov İA: Application of the information technologies in early predicting the severity of atopic dermatitis in children. Int J Pharm Sci & Res 2022; 13(1): 359-68. doi: 10.13040/IJPSR.0975-8232.13(1).359-68.