Comparative analysis of models for assessing asthma severity based on paraclinical studies

Oleh Pihnastyi[1,*,†], Olha Kozhyna[2,†] and Iuliia Karpushenko[3,†]

[1] National Technical University "Kharkiv Polytechnic Institute", 2 Kyrpychova, Kharkiv, 61002, Ukraine
[2] Kharkiv National Medical University, 4 Nauky Avenue, Kharkiv, 61022, Ukraine
[3] Kharkiv National Medical University, 4 Nauky Avenue, Kharkiv, 61022, Ukraine

Abstract

Severe course of bronchial asthma remains a human problem that can lead to death of the patient. To improve diagnostic and prognostic processes in asthma management, this study is conducted using neural network-based models. This paper presents a comparative analysis of models for assessing the severity of bronchial asthma in children based on the paraclinical data. The study included 90 children aged 6 to 18 years including 70 children diagnosed with bronchial asthma and 20 healthy children as a control group. The main biomarker, that is researched in the paper, is serum thymic stromal lymphopoietin. Its concentration is measured by enzyme-linked immunosorbent assay and used as the main parameter in the construction of regression models.

Two predictive models using neural networks are developed in this paper. The first model is focused on thymus stromal lymphopoietin levels as the main predictor of asthma severity, whereas the second model is taken into account a wider range of laboratory parameters including total clinical blood counts, immunoglobulin E levels and measures of immune status. The models were trained and tested on the same paraclinical study dataset. The neural network architecture was standardized to ensure comparability of the models. The results suggest that integrating multiple biomarkers and laboratory examination measures into predictive models may offer more reliable and cost-effective tools for assessing asthma severity, especially in resource-limited settings. The study emphasizes the importance of developing alternative diagnostic methods that are accessible and affordable, especially in countries where the availability of biomarkers such as thymic stromal lymphopoietin may be limited.

Keywords

TSLP, bronchial asthma, child, neural network, multilayer perceptron

1. Introduction

The severe and uncontrolled course of asthma is responsible for several thousand deaths per day worldwide [1]. Asthma is a chronic disease of the respiratory system occurring at all

[1]ITTAP'2024: 4th International Workshop on Information Technologies: Theoretical and Applied Problems, November 20–22, 2024, Ternopil, Ukraine, Opole, Poland
* Corresponding author.
† These authors contributed equally.
pihnastyi@gmail.com (O. Pihnastyi); olga.kozhyna.s@gmail.com (O. Kozhyna); yv.karpushenko@knmu.edu.ua (I. Karpushenko)
0000-0002-5424-9843 (O. Pihnastyi); 0000-0002-4549-6105 (O. Kozhyna); 0000-0002-2196-8817 (I. Karpushenko

ages. The study of bronchial asthma has increased the understanding of the molecular mechanisms underlying the heterogeneity of airway inflammation [2]. One of the key substances, that is involved in the formation of allergic diseases, is thymic stromal lymphopoietin (TSLP). TSLP was first isolated in thymus stromal cells and belongs to the group of cytokines [3]. When respiratory tract epithelium is damaged by viruses, bacteria, allergens, and chemical irritants, TSLP is released, which triggers a pronounced inflammatory response [4]. The paper of A. Berraies et. al. is devoted to the determination of an increased level of TSLP in induced sputum in children with asthma [5]. A similar problem is explored in [6], where the study of biopsy samples of bronchial epithelium of patients with asthma revealed an increased level of TSLP. A correlation between allergen exposure to bronchi in patients with asthma and higher expression of TSLP+???? cells in bronchial epithelium and submucosa is proved [7]. The key role of cytokines IL-25, IL-33 and TSLP, as the main regulators of airway inflammation, in the formation of allergic rhinitis, chronic rhinosinusitis and asthma has been shown [8]. Negative effect of thymic stromal lymphopoietin cytokine on the course of disease was proved in [9, 10, 11]. The drug Tezepelumab, a human monoclonal antibody that is designed to inhibit TSLP, is currently being investigated. The use of the drug provided clinically significant, rapid and sustained relief of asthma exacerbations regardless of asthma phenotype, including patients with severe and uncontrolled asthma [12]. The use of the inhaled drug Ecleralimab, a potent neutralizing antibody fragment against human TSLP, in patients with mild atopic asthma significantly attenuated allergen-induced bronchospasm and airway inflammation [13].

One of the key challenges in the control of bronchial asthma is its heterogeneity in severity and susceptibility to prescribed medications. Modern and effective biomarkers, which include TSLP, can optimize the diagnosis and treatment of patients with asthma and help predict patient functional and clinical outcomes. To determine the laboratory parameters of TSLP in blood, reagents are relatively expensive for patients in countries such as Ukraine and are often unavailable in the laboratory [14]. These factors limit the possibility of widespread use of TSLP for the diagnosis of the disease and require the development of alternative effective and low-cost methods for diagnosing bronchial asthma.

Application of prediction models based on neural network to analyze the data of immunological examination of a patient opens new perspectives for creation of accessible and inexpensive methods of diagnostics of bronchial asthma course severity, that determines the significance and relevance of the present study.

2. Materials and methods

Human TSLP ELISA kit was used for the determination of TSLP level in serum. This method is a 90-minute sandwich immunoassay in a 96-well microtiter plate. The amount of TSLP is measured in picograms per 1 mL of serum (pg/mL). Our study involved 90 children aged 6 to 18 years, divided into two groups. The main group consisted of 70 children diagnosed with bronchial asthma. The control group included 20 healthy children. The average age of children with bronchial asthma is 11 years. The main group included 20 patients with intermittent, 20 patients with mild, 20 patients with moderate persistent and 10 patients with severe persistent asthma. The study was conducted with respect for human rights and in accordance with international ethical requirements; it doesn't violate any scientific ethical

standards and standards of biomedical research [15]. Anamnestic data of patients, clinical symptoms of the disease and indicators of laboratory tests are studied. For every patient, information on 142 factors that could be the cause of bronchial asthma was gathered, processed and analyzed. As a result of preliminary research, factors that can act as basic factors for the creation of alternative methods of asthma diagnosis are identified. Mathematical statistics methods based on neural network is used to build prediction models. These methods are a tool for building dependencies between the degree of asthma severity and: a) the value of TSLP and the degree of bronchial asthma severity; b) the values of factors based on clinical blood tests. Comparative analysis of prediction results using the two types of dependencies will make it possible to assess the accuracy of prediction. As a result of a preliminary study, factors are identified that can act as basic factors for the creation of alternative methods for diagnosing asthma.

In the comparative analysis, the following actions are performed for each patient: 1) general clinical blood test parameters, biochemical studies of TSLP, Ig E and immunogram data are determined; 2) classification of the disease severity degree is performed based on the unified clinical protocol of primary and secondary (specialized) medical care "Bronchial asthma in children" [16].

To analyze the results of the study, two models are built using a neural network: a) the first model for predicting the severity of bronchial asthma is based on the patient immunogram values; b) the second model for predicting the severity of the disease is based on the values of factors for clinical blood analysis. The outcome of the comparative analysis is the prediction accuracy of each of the two models for the tested group of patients. Before the comparative analysis, the patients are divided into two groups, one of which is used for training the neural network and the other for testing.

3. Problem statement

To comparatively analyze the prediction accuracy, two models are built using neural network.

Model Preparation 1. To determine the significance of TSLP in the formation of disease severity, the level of cytokine depending on the severity of AD is analyzed. Evaluation of TSLP levels in children with AD depending on disease severity revealed significant fluctuations of 0.14...149.01 pg/mL and no directly proportional dependence of asthma severity on serum TSLP concentration. On the one hand, in intermittent, mild persistent, and moderate persistent forms of asthma, the median and interquartile intervals of TSLP levels are lower than in controls and did not correlate with disease severity. A probable increase of TSLP level in children with severe persistent course of AD compared with the control group (almost 5-fold increase) and with milder asthma is found, which confirmed the presence of this cytokine in the pathogenesis of some severe forms of AD and substantiated the search for the influence of TSLP on the formation of certain clinical characteristics of the disease. A subgroup of patients with severe asthma showed an increase in TSLP expression despite therapy with high doses of inhaled or oral corticosteroids [17]. To determine the values of TSLP in the pathogenesis of bronchial asthma, the levels of TSLP according to the clinical features of the disease are calculated and used in the present study (Table 1).

Table 1
Dependence of TSLP on clinical features of asthma

Clinical sign of BA		Number of patients	Level of TSLP, pg/ml Median (Q1;Q3)	P1	P2
Manifestation	early (under 3 years)	20	17.93(6.13;40.63)	0.783	0.547
of asthma	late (after 3 years)	50	12.44(5.95;28.01)		0.706
Duration	less than 3 years	16	7.84(5.95;19.93)	0.413	0.272
of disease	more than 3 years	54	13.17(5.04;32.64)		0.836
	less than 7 years	31	7.84(5.22;20.47)	0.133	0.275
	more than 7 years	39	13.94(5.95;36.45)		0.936
Atopy	increased IgE level	59	11.76(4.50;27.01)	0.502	0.676
	normal IgE level	11	13.21(9.58;20.47)		0.555
Clinical	eosinophilia	26	8.71(4.50;16.85)	0.099	0.277
blood count	level of eosinophils < 5 %	44	13.57(5.95;30.28)		0.971
Comorbid	atopic dermatitis	6	36.08(5.04;101.63)	0.195	0.324
conditions	atopic dermatitis	64	11.76(5/22;21.93)		0.472
	allergic rhinitis	39	13.21(5.22;59.69)	0.131	0.731
	no rhinitis	31	8.13(5.22;19.02)		0.159
Allergy	negative	30	15.03(7.37;55.33)	0.027	0.593
heredity	positive	40	7.99(4.50;21.2)		0.218
Asthma	negative	17	17.57(5.95;76.03)	0.148	0.437
heredity	positive	53	11.76(5.22;21.93)		0.340

P1 – comparison between the clinical sign presence and absence groups'
P2 – comparison with the control group

Output parameters of the model are severity degrees of bronchial asthma: SEVERE PERSISTENT, MODERATE PERSISTENT, MILD PERSISTENT, INTERMITTENT. Numerical characteristics of the model output factors are summarized in Table 2.

Preparation Model 2. The general clinical blood test refers to the most common type of blood test and is administered at the first stage of any examination. A blood smear is examined to quantify hematologic parameters: Hemoglobin content (HGB) count; Red blood cell (RBC) count; White Blood Cell (WBC) count; Eosinophils %, Basophils %, Band neutrophils %, Segmented neutrophils %, Lymphocytes %, Monocytes %; Blood platelets (platelets); Erythrocytes Sedimentation Rate (ESR). Determination of total immunoglobulin E (Ig E) is used as a screening test to detect susceptibility to allergic reactions. The selected factors Leucocytes, Neutrophils %, CD3 %, CD4 %, CD8 %, CD16 %, CD22 %, CD25 % refer to indicators of immune status - quantitative and qualitative indicators of cellular and humoral immunity. Numerical statistical characteristics of the input set of factors X_m of the model and observed values Y_α are summarized in Table 2.

Table 2
Numerical characteristics of factors determining the severity of bronchial asthma

Code	Regressor name	m_x, m_y	σ_x, σ_y
X_1	RBC	4.6764	0.2632
X_2	HGB	136.7297	20.115
X_3	WBC	6.6722	1.9
X_4	Eosinophils %	4.0	3.5311
X_5	Basophils %	0.1429	0.3927
X_6	Band neutrophils %	1.2813	0.78
X_7	Segmented neutrophils %	58.9531	11.8631
X_8	Lymphocytes %	31.1094	10.4957
X_9	Monocytes %	4.4688	2.537
X_{10}	ESR	3.8594	1.9435
X_{11}	Ig E	0.8308	0.375
X_{12}	Leucocytes	6.4912	1.3099
X_{13}	Neutrophils %	59.45	7.3449
X_{14}	CD3 %	69.6	2.9983
X_{15}	CD4 %	40.0	1.4318
X_{16}	CD8 %	29.6375	1.6374
X_{17}	CD16 %	12.975	1.565
X_{18}	CD22 %	18.7	1.0654
X_{19}	CD25 %	25.5875	7.7164
Y_1	SEVERE PERSISTENT	0.0444	0.2082
Y_2	MODERATE PERSISTENT	0.3111	0.4657
Y_3	MILD PERSISTENT	0.3111	0.4562
Y_4	INTERMITTENT	0.3333	0.4740

Calculated indicators of correlation coefficients between the model factors X_m, and between the factors of the model X_m and the observed value Y_α are also presented in Table 3.

Table 3
Correlation coefficients values $r_{x_m x_v}$, $r_{y_\alpha x_m}$

	X_1	X_2	X_3	X_4	X_5	X_6	X_7	X_8	X_9	X_{10}
X_2	0.32	-								
X_3	0.06	0.09	-							
X_4	-0.07	-0.14	-0.01	-						

X_5	0.04	0.05	0.17	0.12	-					
X_6	0.11	0.12	0.07	0.03	0.07	-				
X_7	0.25	0.18	0.28	-0.4	0.02	-0.05	-			
X_8	-0.29	-0.22	-0.35	0.09	-0.11	-0.04	-0.91	-		
X_9	0.04	0.2	0.15	0.15	0.03	0.07	-0.29	0.04	-	
X_{10}	0.1	-0.01	0.02	-0.00	0.06	0.58	0.04	-0.11	0.08	-
Y_1	0.11	-0.18	-0.09	0.25	0.07	-0.11	-0.02	-0.04	-0.05	-0.14
Y_2	-0.01	0.09	-0.12	-0.09	0.03	0.13	-0.04	0.06	0.05	0.16
Y_3	-0.02	0.03	0.12	-0.09	-0.13	-0.03	0.23	-0.17	-0.25	0.07
Y_4	-0.05	0.02	0.08	-0.02	0.04	-0,02	-0,16	0,13	0,23	-0,12

In this study, a multilayer perceptron will be used to create each of the two models described above for predicting the severity of bronchial asthma in children. The neural network architecture contains several layers, each of which is connected both to the previous layer, from which it receives data, and to the subsequent layer, which is influenced. The problem of classifying the severity of the course of bronchial asthma for each of the sets of input factors of the first and second models is considered. The calculation of the observed values in each model utilized the same network architecture for the hidden and output layers, with each node having the same activation functions for the two models. Softmax activation function generates the values of the output layer nodes in each model, thus it is guaranteed that the output nodes take positive values and the sum of all output node values is equal to one. The output values of the output factors will be interpreted as the probability of the course degree of bronchial asthma.

4. Prediction model of bronchial asthma severity

Let us consider the construction of comparative prediction models of bronchial asthma severity based on a neural network represented by a multilayer perceptron with the architecture $(M - M_k - Z)$. M is the number of input factors in the prediction model. M_k is the number of nodes in the k-th hidden layer (k=1..L). Z is the number of nodes in the output layer. The minimum number of neurons in the hidden layer is determined from the conditions [18, 19]:

$$M_k \geq \sqrt{MZ}, \quad M_k \geq \frac{1}{2}\frac{N_t}{M\log(N_t)}, \tag{1}$$

for a training sample of size N_t. Hidden layer nodes are characterized by a Sigmoid activation function

$$f(x) = \frac{1}{1 + \exp(-x)}. \quad (2)$$

For the output layer nodes, Softmax function is set as the activation function:

$$f_{Y\alpha}(x_\alpha) = \frac{\exp(-x_\alpha)}{\sum_{\alpha=1}^{Z} \exp(-x_\alpha)}. \quad (3)$$

Softmax function makes it possible to normalize the values of the model output parameters, that makes it possible to predict different degrees of severity of bronchial asthma disease in the studied patients, treating them as probability of disease in accordance with the classification of bronchial asthma by severity of course. Discrete categories in the studied models are treated as a set of values from a common probability distribution. Softmax of the activation function converts the values of the output layer of the neural network into actual discrete probability distributions of the severity of bronchial asthma disease course: SEVERE PERSISTENT, MODERATE PERSISTENT, MILD PERSISTENT, INTERMITTENT.

The neural network architecture for model 1 and model 2 is shown in Figure 1, Figure 2, respectively. The architecture of the models differs in the number of neurons in the input layer. The architecture of hidden layers and output layer in model 1 and model 2 are the same.

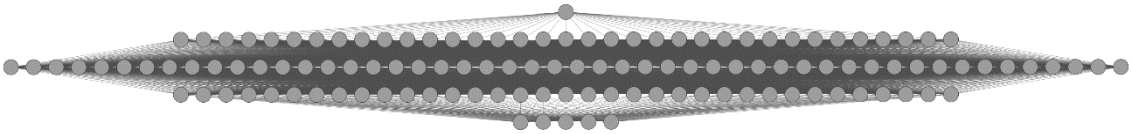

Figure 1: Neural network architecture in a model 1 for predicting the severity of the course of bronchial asthma (M-M1-M2-M3-Z , model input parameters: TSLP).

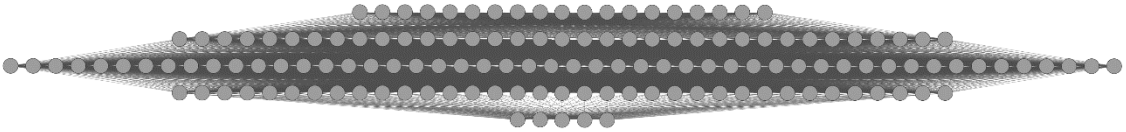

Figure 2: Neural network architecture in a model 2 for predicting the severity of the course of bronchial asthma (M-M1-M2-M3-Z , input parameters of the model: factors of clinical blood analysis).

For each of the models, weights and bias are initialized by a normal distribution of values with parameters. When training neural networks for each of the prediction models, the following hyperparameters are used: a) learning rate $lr = 0.001$; b) number of training epochs: $epoch_{\max} = 20000$.

5. Analyzing the results

A comparative analysis of two models for predicting the bronchial asthma severity in children presents a study of the prediction accuracy. Both models use neural networks but differ in their input parameters. The TSLP-model is based on thymus stromal lymphopoietin level as the main predictor, while the CBT-Model includes a broader set of factors derived from clinical blood tests.

Preliminary analysis of groups of factors [20], with which the severity of bronchial asthma is associated, allowed us to choose the group of factors of clinical blood analysis as the initial set of regressors. A separate study will be devoted to the detailed issue of the factor group selection. The present paper focuses on the comparative analysis of the prediction accuracy for the two models. The first step in the comparative analysis of the two methods for diagnosing the bronchial asthma severity course is the choice of neural network architecture for the prediction models. The TSLP-model uses only one input parameter, the TSLP score in clinical analysis. The CBT-model uses clinical blood test values as input parameters. To ensure training, the weights and bias parameters in both models were initialized using a normal distribution with specified characteristics. The training is performed using hyperparameters: a learning rate of 0.001 and 20000 epochs. A sigmoid activation function is used in the hidden layers to promote nonlinear transformations of the input data, while a Softmax function in the output layer allowed probabilistic predictions of the asthma severity.

For the comparative analysis of the prediction models, the architecture 1-35-50-35-5 (Figure 1) for the TSLP-model and the architecture 19-35-50-35-5 (Figure 2) for the CBT-model are chosen. Two neural network architectures differ in the number of the nodes in the input layer corresponding to the input factors of the models. The number of the nodes in the hidden layers is chosen based on the condition that the training sample containing about 10^5 patients under study will be used in subsequent experiments [21]. Taking into account the formula (1), the number of hidden nodes for the model with one hidden layer is determined by the inequality

$$M_k \geq \frac{1}{2}\frac{10^5}{1\cdot\log\left(10^5\right)} \approx 10^4, \tag{4}$$

which corresponds to 35-50 nodes for each of the three hidden layers for the selected architectures (Figure 1, Figure 2). When training the neural network for each of the prediction models (model 1: TSLP model, Figure 1; model 2: CBT model, Figure 2), the sample for training the neural network is divided into two data sets. The first dataset directly serves to train the neural network and is ~80%, the second dataset (test dataset), which is ~20%, is used to verify the accuracy of the training process. After the training, both models are tested on the validation dataset to evaluate their prediction accuracy. The training process of the neural network for TSLP-model is shown in Figure 3. To demonstrate the neural network training process, four samples with maximum accurancy value are selected containing the above two datasets. The maximum accurancy value is 0.67 for the training process of TSLP-model. Quantitative indicators characterizing the quality of the neural network training process are presented in Table 4.

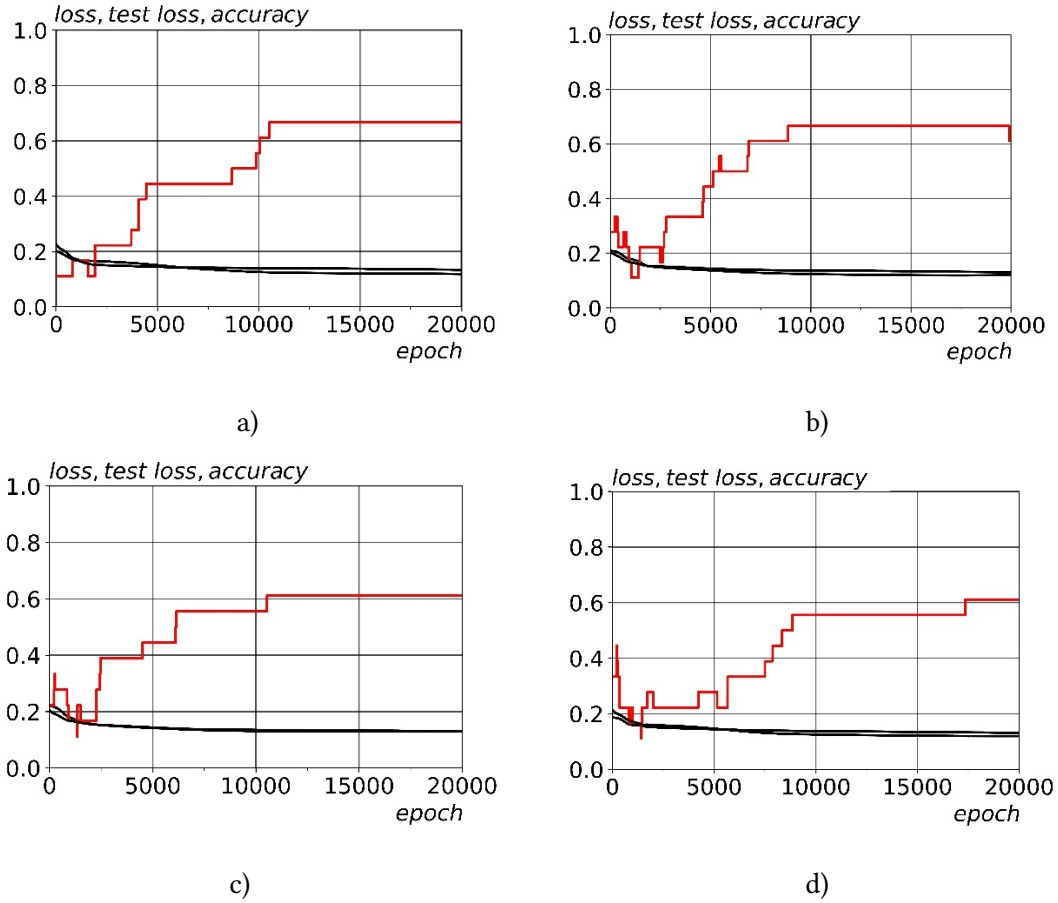

Figure 3: Training a TSLP-model neural network (basic neural network architecture)

Table 4
TSLP-model prediction result (baseline architecture)

	initial					predict				
N#	SEVERE PERSISTENT	MODERATE PERSISTENT	MILD PERSISTENT	INTER MITTENT	HEALTY	SEVERE PERSISTENT	MODERATE PERSISTENT	MILD PERSISTENT	INTER MITTENT	HEALTY
1	0	0	**1**	0	0	0,0133	0,2876	**0,3964**	0,1115	0,1911
2	0	0	**1**	0	0	0,0444	0,1898	0,2184	**0,4214**	0,1260
3	0	**1**	0	0	0	0,2818	0,1769	0,0582	0,0863	**0,3968**
4	0	0	0	**1**	0	0,0348	0,2078	0,2463	**0,4005**	0,1106
5	0	0	0	**1**	0	0,0161	0,3009	**0,3888**	0,1774	0,1167
6	0	0	**1**	0	0	0,0674	0,1789	0,1887	**0,3897**	0,1753
7	0	0	0	**1**	0	0,2477	0,1733	0,0669	0,1007	**0,4115**
8	0	**1**	0	0	0	0,0161	**0,3009**	0,3888	0,1774	0,1167
9	**1**	0	0	0	0	0,1077	0,1773	0,1537	**0,2910**	0,2702
10	0	0	**1**	0	0	0,0844	0,1779	0,1737	**0,3485**	0,2155
…	…	…	…	…	…	…	…	**…**	**…**	…

An exact match is presented for ~30% of the studied patients. In ~80% of cases, the TSLP-model detects either an exact match or a neighboring group in the qualification table, which is a reasonably good prediction result for the TSLP-model.

For comparative analysis, the training process of the neural network for TSLP model is shown in Figure 4. As for the TSLP-model, the CBT-model shows a maximum accurancy value of 0.67 for the training process, equal to the value obtained for the TSLP-model. This is a good enough result to suggest the use of the CBT-model as an alternative to the TSLP model for prediagnosis of bronchial asthma severity.

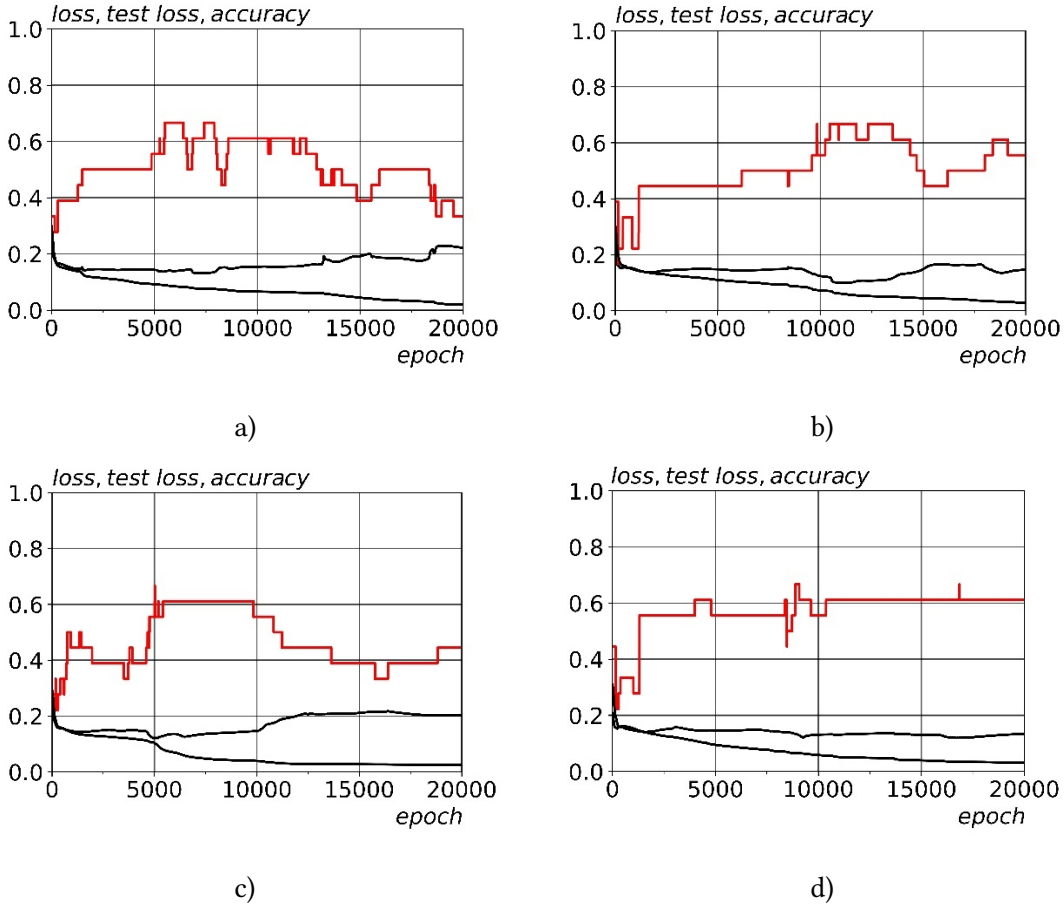

Figure 4 Training a neural network of a CBT-model (basic architecture of a neural network)

One difference is that for a given number of epochs (for each of the model $epoch_{\max} = 20000$), loss, accurancy and test loss functions asymptotically tend to the value determined by the model parameters, while the learning process for the CBT-model neural network is not steady-state. It should also be noted that for the TSLP-model the loss and test loss functions asymptotically approach each other. Such behavior is not observed for the CBT model, which also indicates that the learning process for the CBT-model should contain a larger number of epochs. The latter circumstance is to some extent explained by the fact that the CBT-model contains significantly more input factors than the TSLP-model.

For a comparative analysis of the two prediction models, quantitative indicators characterizing the quality of the training process of the neural network of the CBT-model are presented in Table 5.

Table 5
CBT-model prediction results

	initial					predict				
N#	SEVERE PERSISTENT	MODERATE PERSISTENT	MILD PERSISTENT	INTER MITTENT	HEALTY	SEVERE PERSISTENT	MODERATE PERSISTENT	MILD PERSISTENT	INTER MITTENT	HEALTY
1	0	0	0	**1**	0	0,0018	0,0649	0,0387	**0,8931**	0,0015
2	0	0	**1**	0	0	0,1549	**0,3465**	0,2732	0,2067	0,0187
3	0	0	0	**1**	0	0,0312	0,0658	0,0474	**0,7738**	0,0817
4	0	0	0	0	**1**	0,0051	0,0139	0,0053	0,0838	**0,8919**
5	0	0	0	**1**	0	0,0080	0,0053	0,0018	**0,9835**	0,0014
6	0	**1**	0	0	0	0,1524	**0,3559**	0,2564	0,2162	0,0191
7	0	0	**1**	0	0	0,0011	0,0567	**0,9387**	0,0034	0,0001
8	0	0	**1**	0	0	0,1524	**0,3559**	0,2564	0,2163	0,0191
9	**1**	0	0	0	0	**0,8815**	0,0032	0,0329	0,0582	0,0241
10	0	0	**1**	0	0	0,1519	**0,3575**	0,2560	0,2156	0,0190
…	…	…	…	…	…	…	…	**…**	**…**	…

An exact match in the present study for the training and test dataset is found for ~70% of the patients studied. In each case, the CBT-model predicted either an exact match or a neighboring group in the qualification table, which is a rather unexpected result obtained. The second result achieved is also noteworthy. The values of probability of predicting the severity of bronchial asthma disease course for CBT-model is much higher, reaching the value from 0.8 to 1.0 for a rather large group of analyzed patients. The obtained prediction results for the CBT-model are explained by a large number of input factors obtained from clinical blood tests.

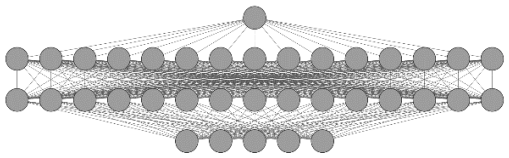

Figure 5: Neural network architecture in a TSLP-model for predicting the severity of the course of bronchial asthma (neural network architecture 1-15-15-5)

In addition to this study, let us consider the effect of changing the neural network architecture on the quality of the model for predicting the severity of bronchial asthma disease. The process of training the neural network for TSLP model with 1-15-15-5 neural network architecture (Figure 5) is shown in Figure 6.

As for the basic architecture, four samples with the maximum accuracy value were selected to demonstrate the process of training the neural network. When training the neural network, the maximum accuracy value decreased slightly. For the number of epochs defined in the base case, the neural network training process did not reach steady-state. Quantitative indicators characterizing the quality of the neural network training process are presented in Table 6.

An exact match is presented for ~20% of the study patients, which is lower than in the base case. Also, as in the base case, for ~80% of cases the TSLP-model identifies either an exact match or a neighboring group in the qualification table.

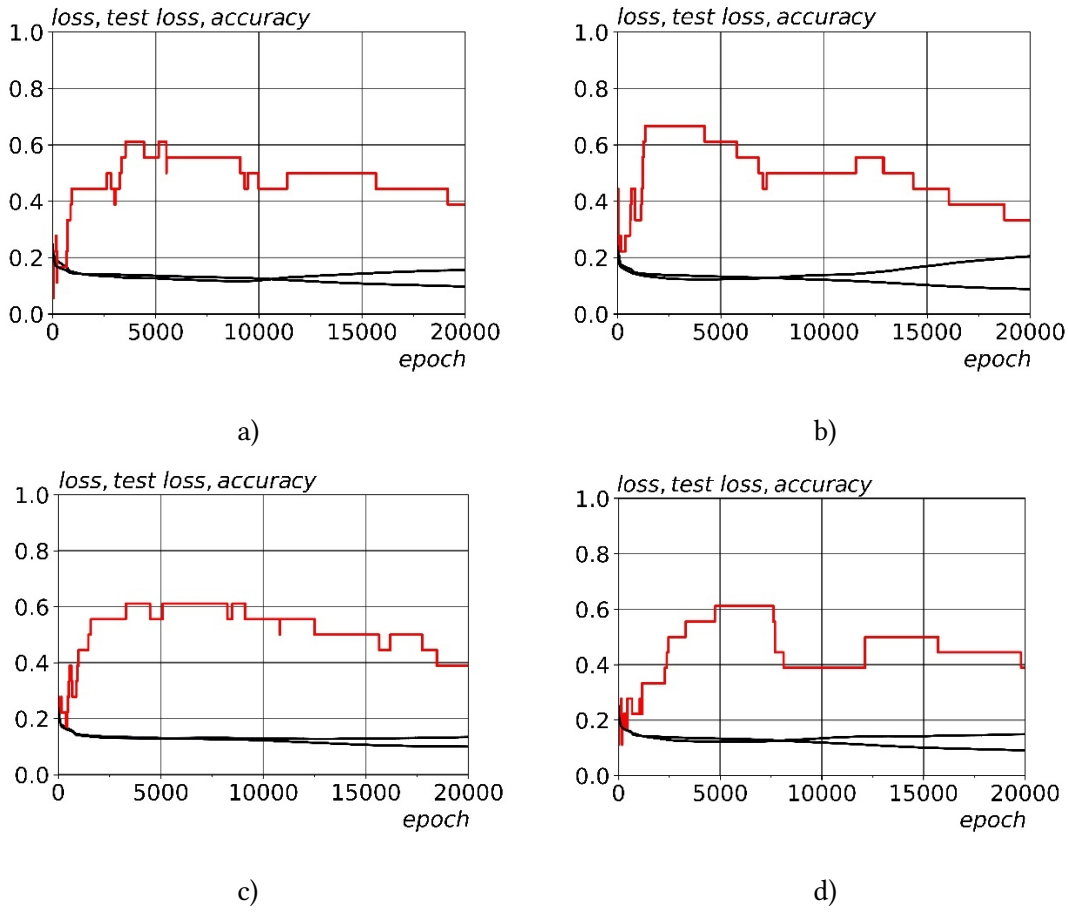

Figure 6: Training a TSLP-model neural network (neural network architecture 1-15-15-5)

Table 6
TSLP-model prediction result (neural network architecture 1-15-15-5)

	initial					predict				
N#	SEVERE PERSISTENT	MODERATE PERSISTENT	MILD PERSISTENT	INTER MITTENT	HEALTY	SEVERE PERSISTENT	MODERATE PERSISTENT	MILD PERSISTENT	INTER MITTENT	HEALTY
1	0	0	**1**	0	0	0,0093	0,2475	**0,3546**	0,2121	0,1764
2	0	0	**1**	0	0	0,0480	0,1887	0,2110	**0,4347**	0,1176
3	0	**1**	0	0	0	0,2643	0,2137	0,0559	0,0754	**0,3907**
4	0	0	0	**1**	0	0,0346	0,2143	0,2390	**0,4136**	0,0985
5	0	0	0	**1**	0	0,0112	0,3065	**0,4011**	0,1868	0,0944
6	0	0	**1**	0	0	0,0778	0,1674	0,1885	**0,3934**	0,1728
7	0	0	0	**1**	0	0,2372	0,1907	0,0676	0,0881	**0,4164**
8	0	**1**	0	0	0	0,0112	0,3065	**0,4011**	0,1868	0,0944
9	**1**	0	0	0	0	0,1225	0,1574	0,1624	**0,2820**	0,2757
10	0	0	**1**	0	0	0,0978	0,1617	0,1782	**0,3457**	0,2165
…	…	…	…	…	…	…	…	**…**	**…**	…

The comparative analysis shows that the CBT model, which incorporates multiple clinical factors, is not inferior in predicting the quality of the TLSP-model based solely on the TSLP level. Although TSLP is an important biomarker associated with asthma severity, it does not encompass the entire multifactorial nature of the disease. The sufficiently high accuracy of the CBT model indicates that the integration of multiple clinical indicators provides a more complete picture of disease severity.

In addition, the sensitivity and specificity of both models were evaluated to better understand their diagnostic capabilities. The CBT-model showed higher sensitivity in detecting severe and moderate cases of asthma, while maintaining an acceptable level of specificity. The latter indicates that the CBT-model is an alternative for clinical applications where accurate determination of asthma severity plays a key role in treatment planning.

In conclusion, comparative model analysis provides valuable results integrating different clinical parameters, providing an accurate and reliable method for predicting the severity of bronchial asthma in children. This approach is in line with the general trend in medicine towards precision diagnosis and personalized treatment.

6. Conclusion

The present study successfully demonstrated the feasibility of using neural network-based predictive models to determine the severity of bronchial asthma in children by analyzing various clinical and immunological parameters. Two models developed, one based on thymic stromal lymphopoietin (TSLP) levels and the other on factors of the total clinical blood count, provided a clear indication of the correlation between model regressors and disease severity. Although there was no direct proportional relationship between TSLP levels and asthma severity in all cases, the TSLP-based model emphasized the potential of TSLP as a biomarker, especially in severe asthma. On the other hand, the model based on total clinical blood count

showed significant predictive accuracy, offering an alternative method for assessing disease severity.

The comparative analysis of these models demonstrates that, although each model has its own merits, the integration of several biomarkers and clinical parameters can improve the accuracy and reliability of asthma severity predictions. It is important to emphasize that the model based on clinical blood count factors demonstrated a prediction accuracy commensurate with that based on thymic stromal lymphopoietin (TSLP) levels, which supports the hypothesis that this model can be used as one method of reasonably accurate diagnosis of asthma severity.

In the absence of TSLP reagents in clinical institutions, a prediction model based on the results of the general clinical blood test can be used to diagnose the severity of the course of bronchial asthma quite effectively. If TSLP-based paraclinical tests are available, the developed diagnostic models can act as verification of TSLP laboratory test results.

The fact that the TSLP model relies on a single biomarker limits its ability to predict asthma severity across the disease spectrum. In addition, it should be considered that the models were trained on a relatively small dataset for comparative analysis of prediction performance. Future research could focus on expanding the dataset and incorporating additional biomarkers and laboratory examination scores to further improve the prediction accuracy of the models. In addition, investigating alternative neural network architectures, such as convolutional or recurrent networks, may provide a deeper understanding of the temporal dynamics of asthma severity. Integrating data on disease dynamics over time will improve the ability of models to predict changes in asthma severity and facilitate the development of personalized treatment strategies.

The results emphasize the importance of developing cost-effective and accessible diagnostic tools tailored to the specific needs of resource-limited regions. Further research and refinement of these models could lead to improved, personalized treatment plans, ultimately improving patient outcomes and reducing the burden of bronchial asthma on health care systems.

References

[1] Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2024, https://ginasthma.org/reports/.

[2] M. E. Kuruvilla, F. Eun-Hyung Lee, G. B. Lee, Understanding asthma phenotypes, endotypes, and mechanisms of disease, Clin Rev Allergy Immunol, 2019, vol. 56(2), pp. 219–233, doi: 10.1007/s12016-018-8712-1.

[3] G. Varricchi, A. Pecoraro, G. Marone, G. Criscuolo, G. Spadaro, A. Genovese et al, Thymic stromal lymphopoietin isoforms, Inflammatory Disorders, and Cancer, Frontiers in Immunology, 2018, 9, doi: 10.3389/fimmu.2018.01595.

[4] G. M. Gauvreau, R. Sehmi, C. S. Ambrose, J. M. Griffiths, Thymic stromal lymphopoietin: its role and potential as a therapeutic target in asthma, Expert Opin Ther Targets, 2020, vol. 24(8), pp. 777–792, doi: 10.1080/14728222.2020.1783242.

[5] A. Berraies, B. Hamdi, J. Ammar, K. Hamzaoui, A. Hamzaoui, Increased expression of thymic stromal lymphopoietin in induced sputum from asthmatic children, Immunol. Lett, 2016, vol. 178, pp. 85–91, https://doi.org/10.1016/j.imlet.2016.08.004.

[6] D. Al-Sajee, R. Sehmi, T.J. Hawke et al, Expression of IL-33 and TSLP and their receptors in asthmatic airways after inhaled allergen challenge, Am J Respir Crit Care Med, 2018, vol.198(6), pp. 805–807, doi: 10.1164/rccm.201712-2468LE.
[7] W. Wang, Y. Li, Z. Lv, Y. Chen, Y. Li, et al, Bronchial allergen challenge of patients with atopic asthma triggers an alarmin (IL-33, TSLP, and IL-25) response in the airways epithelium and submucosa, J Immunol, 2018, vol. 201(8), pp. 2221–2231, https://doi.org/10.4049/jimmunol.1800709.
[8] H. Hong, S. Liao, F. Chen, Q. Yang, De-Yun Wang, Role of IL-25, IL-33, and TSLP in triggering united airway diseases toward type 2 inflammation, Allergy, 2020, vol.75(11), pp. 2794-2804, doi: 10.1111/all.14526.
[9] H. Guo, X. Ji, G.Yang, Y. Jin, Abnormal thymic stromal lymphopoietin expression in the gastrointestinal mucosa of patients with eosinophilic gastroenteritis, Jornal de Pediatria, 2020, vol. 96(3), pp. 350-355, doi: 10.1016/j.jpedp.2019.03.002.
[10] S. Colicino, D. Munblit, C. Minelli, A. Custovic, P. Cullinan, Validation of childhood asthma predictive tools: a systematic review, Clin Exp Allergy, 2019; 49(4), pp. 410- 418, doi: 10.1111/cea.13336.
[11] O. Kozhyna, O. Pihnastyi, Covariance coefficients factors from a clinical study of the severity of bronchial asthma in children of the Kharkov region, 2017, Mendeley Data, 1, 2019.
[12] J. R. Parnes, N. A. Molfino, G. Colice, U. Martin, J. Corren et al, Targeting TSLP in asthma, J Asthma Allergy, 2022, vol.15, pp. 749-765, doi: 10.2147/JAA.S275039.
[13] G. Gauvreau, J. M. Hohlfeld, J. M. FitzGerald, L.-P. Boulet, D. W. Cockcroft et al, Inhaled anti-TSLP antibody fragment, ecleralimab, blocks responses to allergen in mild asthma, Eur Respir J, 2023, vol. 61(3):2201193, doi: 10.1183/13993003.01193-2022.
[14] https://www.elkbiotech.com/pro/ELK1083
[15] UNESCO.ORG, Universal Declaration on Bioethics and Human Rights, 2005, http://portal.unesco.org/en/ev.php. 2005.
[16] https://zakon.rada.gov.ua/rada/show/v2856282-21
[17] A. Shikotra, D. F. Choy, C. M. Ohri, E. Doran, C. Butler et al, Increased expression of immunoreactive thymic stromal lymphopoietin in patients with severe asthma, J Allergy Clin Immunol, 2012, vol.129(1):104-11.e1-9, doi: 10.1016/j.jaci.2011.08.031.
[18] M. Paul, M. Chakraborty, Observation on training neural network for diagnosing schizophrenia, International Journal of Advanced Research in Computer Science, 2018, vol. 9(1), pp. 163–166, http://dx.doi.org/10.26483/ijarcs.v9i1.5279.
[19] D. Stathakis, How many hidden layers and nodes? International Journal of Remote Sensing, 2009, vol. 30, pp. 2133-2147, doi:10.1080/01431160802549278.
[20] O. Kozhyna, O. Pihnastyi, Data Structure of Clinical Research, Human Health & Disease, 2019, vol. 3(9), p. 71-79, http://dx.doi.org/10.2139/ssrn.3336301.
[21] V. Klymenko, O. Kozhyna, K. Zemlianskyi, Prevalence of bronchial asthma symptomatic manifestation among children of Kharkiv, The world of medicine and biology, 2019, vol. 2(68), p.61-65, doi:10.26.724/2079-8334-2019-2-68-61-65.