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INVESTIGATION OF DATA ON MORPHOLOGICAL CLASSIFICATION OF CLINICAL AND HEMATOLOGICAL SYNDROMES BASED ON MACHINE LEARNING ALGORITHMS

МАШИНАЛЫҚ ОҚЫТУ АЛГОРИТМДЕРІНЕ НЕГІЗДЕЛГЕН КЛИНИКАЛЫҚ-ГЕМАТОЛОГИЯЛЫҚ СИНДРОМДАРДЫҢ МОРФОЛОГИЯЛЫҚ ЖІКТЕМЕ ДЕРЕКТЕРІН ЗЕРТТЕУ

ИССЛЕДОВАНИЕ ДАННЫХ МОРФОЛОГИЧЕСКОЙ КЛАССИФИКАЦИИ КЛИНИКО-ГЕМАТОЛОГИЧЕСКИХ СИНДРОМОВ НА ОСНОВЕ АЛГОРИТМОВ МАШИННОГО ОБУЧЕНИЯ

Abstract. *Currently, the greatest attention is paid to the problem of the development and application of medical information systems, their integration in the direction of building a single information space. There is a need to develop decision support systems that are direct «assistants» of doctors in the medical and diagnostic process and should find their place in integrated systems. The urgency of the problem lies in the need to develop intelligent medical systems based on effective methods, algorithms and models to support medical decision-making in conditions of incompleteness and uncertainty of the initial data of the medical and technological process, allowing to ensure high adequacy and validity of decisions made in conditions of limited time resources. To solve this problem, this article proposes a study of data on the morphological classification of clinical and hematological syndromes based on machine learning algorithms. The use of machine learning algorithms for indicators of clinical and hematological syndromes will increase the effectiveness of differential diagnosis and apply it to the development of algorithmic and software for an intelligent system to support clinical decision-making.*

Keywords: *clinical decision support, differential diagnosis, clinical and hematological syndromes, machine learning algorithms, neural networks, medical information systems.*

Аңдатпа. *Қазіргі уақытта ақпараттық медициналық жүйелерді әзірлеу және қолдану, оларды бірыңғай ақпараттық кеңістікті құру бағытында интеграциялау мәселесіне көп көңіл бөлінеді. Емдеу-диагностикалық процесте дәрігерлердің тікелей «көмекшілері» болып табылатын және интеграцияланған жүйелерде өз орнын табуы керек шешім қабылдауды қолдау жүйелерін әзірлеу қажеттілігі туындайды. Мәселенің өзектілігі уақытша ресурстардың шектеулілігі жағдайында қабылданатын шешімдердің жоғары барабарлығы мен негізділігін қамтамасыз етуге мүмкіндік беретін медициналық-технологиялық процестің бастапқы деректерінің толық еместігі мен белгісіздігі жағдайында медициналық шешімдерді қабылдауды қолдаудың тиімді әдістері, алгоритмдері мен модельдері негізінде медициналық мақсаттағы интеллектуалды жүйелерді әзірлеу қажеттілігінде жатыр. Бұл мәселені шешу үшін осы мақалада машиналық оқыту алгоритмдеріне негізделген клиникалық-гематологиялық синдромдардың морфологиялық классификациясының деректерін зерттеу ұсынылған. Клиникалық-гематологиялық синдромдардың* *көрсеткіштері үшін машиналық оқыту алгоритмдерін қолдану дифференциалды диагностиканың тиімділігін арттыруға және оны клиникалық шешімдерді қабылдауды қолдаудың интеллектуалды жүйесінің алгоритмдік және бағдарламалық қамтамасыз етуін әзірлеу үшін қолдануға мүмкіндік береді.*

Түйін сөздер: *клиникалық шешімдерді қолдау, дифференциалды диагностика, клиникалық-гематологиялық синдромдар, машиналық оқыту алгоритмдері, нейрондық желілер, медициналық ақпараттық жүйелер.*

Аннотация. *В настоящее время наибольшее внимание уделяется проблеме разработки и применения информационных медицинских систем, их интеграции в направлении построения единого информационного пространства. Возникает необходимость разработки систем поддержки принятия решений, которые являются непосредственными «помощниками» врачей в лечебно-диагностическом процессе и должны находить свое место в интегрированных системах. Актуальность проблемы заключается в необходимости разработки интеллектуальных систем медицинского назначения на основе эффективных методов, алгоритмов и моделей поддержки приятия медицинского решений в условиях неполноты и неопределенности исходных данных медико-технологического процесса, позволяющих обеспечивать высокую адекватность и обоснованность принимаемых решений в условиях ограниченности временных ресурсов. Для решения этой проблемы в данной статье предложено исследование данных морфологической классификации клинико-гематологических синдромов на основе алгоритмов машинного обучения. Применение алгоритмов машинного обучения для показателей клинико-гематологических синдромов позволит повысить эффективность дифференциальной диагностики и применить его для разработки алгоритмического и программного обеспечения интеллектуальной системы поддержки принятия клинических решений.*

Ключевые слова: *поддержка принятия клинических решений, дифференциальное диагностирование, клинико-гематологические синдромы, алгоритмы машинного обучения, нейронные сети, медицинские информационные системы.*

Introduction. Taking into account all the recent unfavorable events in the world, including the global pandemic, quarantine restrictions, and economic shocks, the development of the healthcare sector is one of the top priorities of any country.

In this regard, Kazakhstan, like any other country, needs to improve the efficiency of the health sector and the availability of medical care for the entire population, which in turn can be achieved only through digitalization, namely the integration of the main activities of the health sector with information systems, the use of mobile digital applications, the introduction of electronic health passports and the transition to "paperless" hospitals.

As part of the digitalization of Kazakhstan's healthcare since 2020, almost all (or rather 94.69%) Kazakhstanis have received an electronic health passport, which stores their medical history and is available to the polyclinic, ambulance, hospital. Passport data is updated on a weekly basis with data from all medical institutions.

This research is aimed at developing a software package for the diagnosis of clinical and hematological syndromes (CDS) for an electronic passport, which allows automating the process of PPCR based on differential diagnosis algorithms and models of intelligent analysis of medical data.

Anemia is also widespread in Kazakhstan, as evidenced by the results of National Nutrition Studies conducted by the Kazakh Academy of Nutrition. The results of the study showed that more than 40% of school-age children suffer from anemia. The prevalence of anemia is especially high (49.4%) among children aged 12-14 years, as well as among women of reproductive age (48.2%) and among children aged 6-59 months (47.4%). It turned out that in Kazakhstan almost every third man (28.1%) also suffers from anemia. The prevalence of anemia per the entire population is 41.9%. This means that 6.5 million people in Kazakhstan suffer from anemia [1].

Literature review. Artificial neural networks are statistical methods that mimic complex neural connections, simulating the learning dynamics of the human brain. They play a fundamental role in clinical decision-making, although their success depends on good integration with clinical protocols. ANN have shown excellent aptitude in learning the relationships between the input/output mapping from a given dataset, without any prior information or assumptions about the statistical distribution of the data [2]. Artificial Neural Networks (ANNs) have proven to be effective for modeling decision-making problems in medicine, including diagnostics, prediction, resource allocation, and cost reduction problems. Research using ANNs to solve problems in the field of medicine is regularly expanded and continues to grow rapidly [3].

New inventions are being added to the arsenal of available medical tools that help diagnose and treat diseases. The evolution of AI in clinical medicine is traced, starting with fuzzy logic and expert systems, then to artificial neural networks and more complex architectures, moving towards the support of vector machines, feature engineering and natural language processing [4].

Deep learning methods are increasingly used to solve problems in medicine and healthcare. Thus, the article [5] presents the basics of deep learning from an epidemiological point of view. It covers the core concepts of machine learning (overfitting, regularization, hyperparameters), explains several fundamental deep learning architectures (Convolutional Neural Networks, Recurrent Neural Networks), and summarizes model training, evaluation, and deployment.

Scientists in [6] give an overview of recent applications based on artificial neural networks used in the field of medicine, from the databases PsycINFO, Google Scholar, PubMed, and the library of the University of Rhode Island. Data from several studies show that artificial neural networks can be used to diagnose, predict, and treat many diseases.

The use of neural networks in medicine can be divided into two types: automatic diagnosis and medical assistance. Considering the number of patients per doctor, neural networks can be used to diagnose diseases related to the vascular system, heart, brain, spine, head, neck, and tumors/cancer in three areas: vascular and interventional radiology, interventional cardiology, and neuroradiology [7].

Given the rapid development of technology, the authors [8] argue that the use of AI in medicine shows promising results in the context of patient care. It is especially important to closely monitor this problem and conduct further research to fully explore the potential of ML, ANN, and DL, as well as to introduce additional applications into clinical use in the future.

According to the authors of [9], general nuclear medicine may benefit from more advanced deep learning applications for classification, detection, localization, segmentation, quantification, and radiomic feature extraction utilizing 3D CNNs.

Medicine is characterized by its inherent uncertainty, i.e., the difficulty of identifying and obtaining exact outcomes from available data. Electronic Health Records aim to improve the exactitude of health management, for instance using automatic data recording techniques or the integration of structured as well as unstructured data. However, this data is far from perfect and is usually noisy, implying that epistemic uncertainty is almost always present in all biomedical research fields. This impairs the correct use and interpretation of the data not only by health professionals but also in modeling techniques and AI models incorporated in professional recommender systems [10].

The study by the authors of [11] proposes a novel end-to-end hierarchical graph neural network with interpretable modules is proposed, which learns structural features at multiple scales and incorporates a soft mask layer in extracting subgraphs that contribute to classification.

In [12], the diagnosis of cancer in breast cells is considered using advanced methods such as deep complex neural networks and data mining, which can significantly improve the accuracy and speed of disease detection.

The authors of [13] used various machine learning algorithms, such as k-nearest neighbors, support vector machine, decision tree, self-organizing fuzzy logic, and convolutional neural networks, to classify breast tissues with high accuracy. Their study demonstrated the benefits of using convolutional neural networks for cancer detection and tissue classification. Compared to traditional methods, convolutional neural networks gave more reliable and better results.

According to the results of the study [14], the efficiency of an intelligent cloud health platform, which is based on the deep neural network, is 10.5% higher than that of a conventional cloud health platform and is more popular among citizens. In the development of the medicine cloud healthcare system, in combination with the technology of deep neural networks, big data analysis technology was used.

In the article [15], the creation of an artificial intelligence (AI) model is performed using a publicly available dataset of molecules and their pIC50 values. Artificial and convolutional neural networks (ANN and CNN) are used as modeling algorithms. Three approaches are being tested - simulation using only molecular properties (MP), encoded representation of the SMILES molecule, and a combination of both input data types.

Authors of work [16] developed an integrative forecasting tool SUPREME using graph neural network methods, where several data modalities are combined into graphically structured data. The study [17] proposes a novel Heterogeneous Graph Convolutional Neural Network (HGCNN) for processing complex brain fMRI data at regional and interregional levels. Frequently used graph neural networks, their training methods and common datasets for them are described in detail in [18].

The study [19] proposes an artificial intelligence framework for predicting blood pressure using deep convolutional neural networks. During the study, pulse wave signals were extracted. They then trained and compared nine artificial neural networks and selected the prediction model with the best performance, with a high true prediction ratio.

Convolutional neural networks were also used in [20] for the classification of medical images. The CNN is optimized using different versions of the evolutionary algorithm. The goal is to increase the performance of the algorithm to more than 90%.

Another work [21] proposes the use of neural networks to accelerate the process of early disease detection, in particular cancer. Here are several new adaptive neural networks that integrate genomic knowledge into their architecture, improving diagnostic efficiency and computational speed while reducing computational costs.

In article [22] authors use machine learning and artificial neural network algorithms are used to estimate gender by parameters obtained from the upper dental arcade. In the course of the study, the scientists obtained a high level of accuracy as a result of 500 times training with the Multilayer Perceptron Classifier (MLCP), which is an artificial neural network (ANN) model. In [23], a special convolutional neural network was developed to identify key breast features that are commonly used in plastic surgery to assess symmetry. As a result, the trained program was successfully able to detect the key signs by almost 100%.

Quantum support vector classifiers and quantum neural networks have been trained on various sets of clinical and real-world data. This includes research on the creation of new molecular objects as drug candidates, diagnostics based on the classification of medical images, prediction of patient resistance, prediction of treatment effectiveness and adaptation of radiation therapy [24].

In [25], the Enhanced Leader-Based Hybrid Optimization (EHLBO) algorithm is used to tune the parameters of compressed convolutional neural networks. The ECCHLO model is being explored and tested on four datasets, namely: SARS-COV-2, Covid-19 X-ray database, Covid-CT datasets, and Covid-19 images. The accuracy of these four datasets is 99.6%, 99.5%, 99.3% and 100% respectively, which is higher than other methods.

The authors [26], taking into account the large amount of complex morphology and the lack of publicly available sets of visual data of Tibetan medical materials, proposed an effective mechanism of interdimensional attention, the Dual-Kernel Split Attention module (DKSA), which can be integrated into various backbone architectures to improve model performance. In work [27] described the development of a branched visible neural network that combines two heterogeneous neural networks. The structure of the first neural network reflects the hierarchical organization of cellular subsystems. During training, this neural network learns the behavior of cellular subsystems. The second neural network is fully connected and models the chemical structure of each drug. These two neural networks are connected to a series of small, fully connected layers.

Research methods. An experimental study of the algorithm of morphological classification of clinical and hematological syndromes based on neural networks was implemented on the basis of the following indicators of blood and gender of the patient:

• Gender - gender (0 - male, 1 - female)
• Hemoglobin - hemoglobin content (g/dl)
• MCH - average hemoglobin in the cell (pg)
• MCHC - average erythrocyte hemoglobin concentration (%)
• MCV - average erythrocyte volume (fl)
• Result - result (0 - no anemia, 1 - there is anemia)

The distributions and values of the data are shown in the diagrams in Figure 1.

When a patient's hemoglobin is below normal, it is important to determine whether the red blood cells have a normal size and whether the concentration of hemoglobin in them is normal. These measurements, known as red blood cell indices, provide important information about different types of anemia.

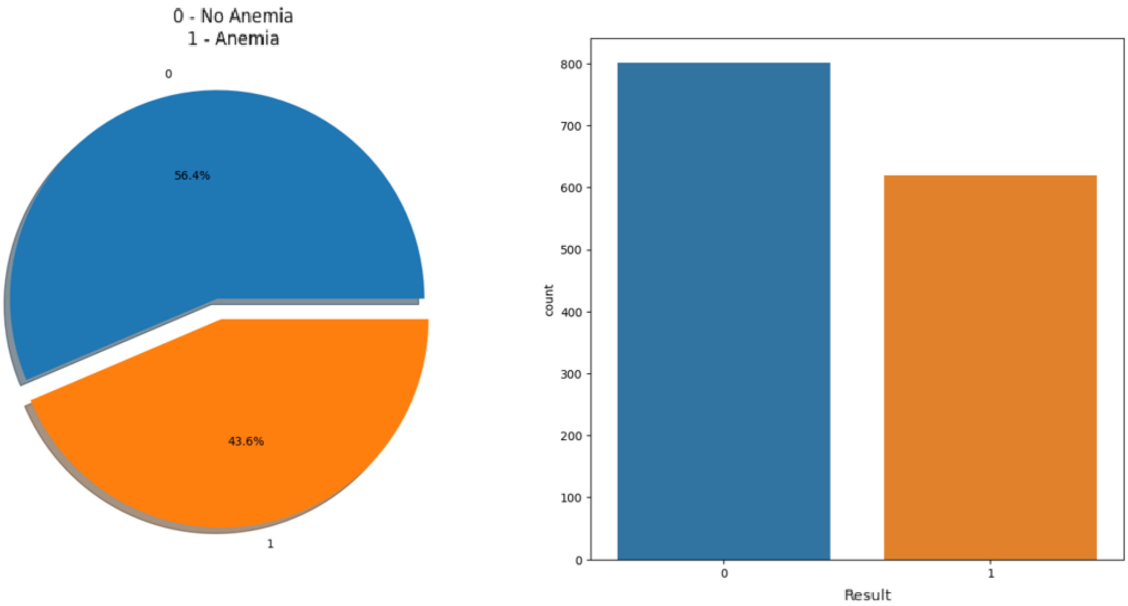

Figure 1. Distributions and values of data by gender

Mean Corpuscular Volume (MCV) measures the average size of individual red blood cells. If the MCV is low, the cells are microcytic or less than normal. Microcytic erythrocytes are observed in iron deficiency anemia, lead poisoning and genetic diseases of thalassemia major and minor. If the MCV is high, the cells are macrocytic or larger than usual. Macrocytic erythrocytes are associated with pernicious anemia and folic acid deficiency. If the MCV is within the normal range, the cells are called normocytic. A patient with anemia will have normocytic anemia as a result of acute bleeding.

Mean Corpuscular hemoglobin (MCH) measures the amount or mass of hemoglobin present in a single red blood cell. The result is reported by a very small weight, called a picogram (pg).

The distributions and values of hemoglobin and MCH are shown in the diagrams of Figure 2.

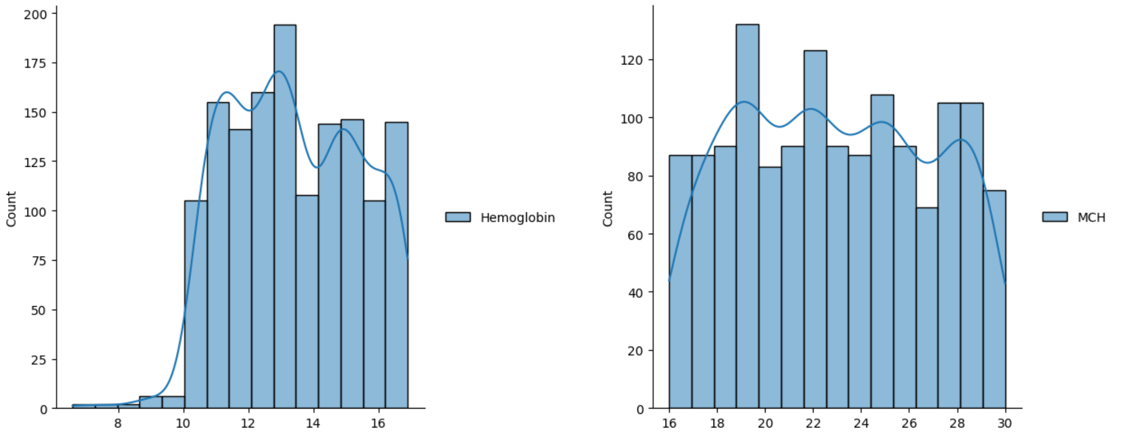

Figure 2. Distributions and values of hemoglobin and MCH index

The mean corpuscular hemoglobin Concentration (MCHC) measures the proportion of each cell occupied by hemoglobin. MCH and MCHC are used to assess whether red blood cells are normochromic, hypochromic or hyperchromic. MCHC less than 32% or MCH less than 27%. indicates a deficiency of hemoglobin in red blood cells. This situation is most often observed with iron deficiency anemia.

Normal values of MCV: Men: 80-98 fl (femtoliters), Women: 96-108 fl; MCH – 17-31 pg (picograms); MCHC - 32-36%.

The distributions and values of the MCH and MCV indicators are shown in the diagrams in Figure 3.

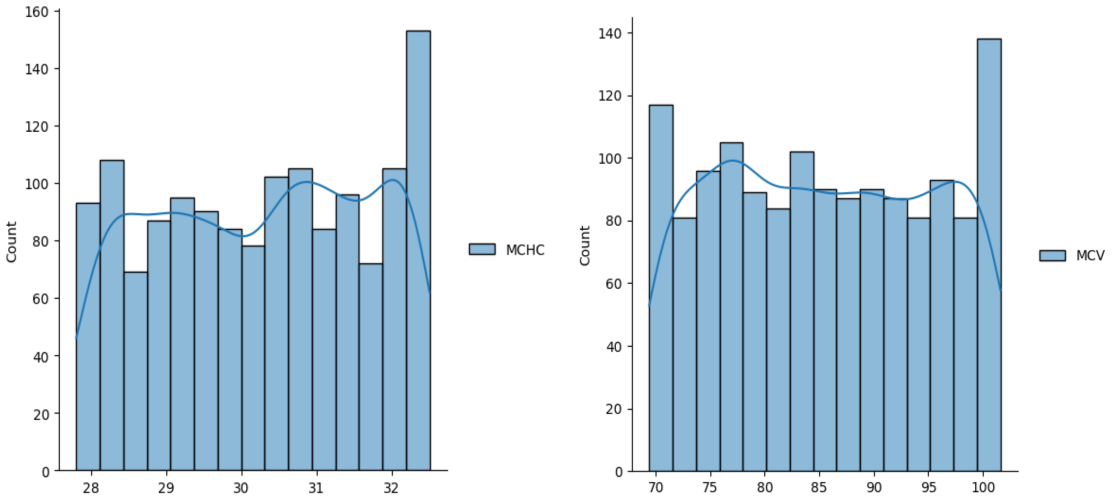

Figure 3. Distributions and values of MCHC and MCV indicators

Thus, the data contains a sufficient number of both positive and negative results for training. The input indicators are mostly homogeneous and balanced.

For a better study of the initial data, a correlation matrix was constructed, establishing the dependence of the result (the presence of anemia) on the initial variables (indicators of biochemical blood analysis). The resulting correlation matrix is shown in Figure 4.

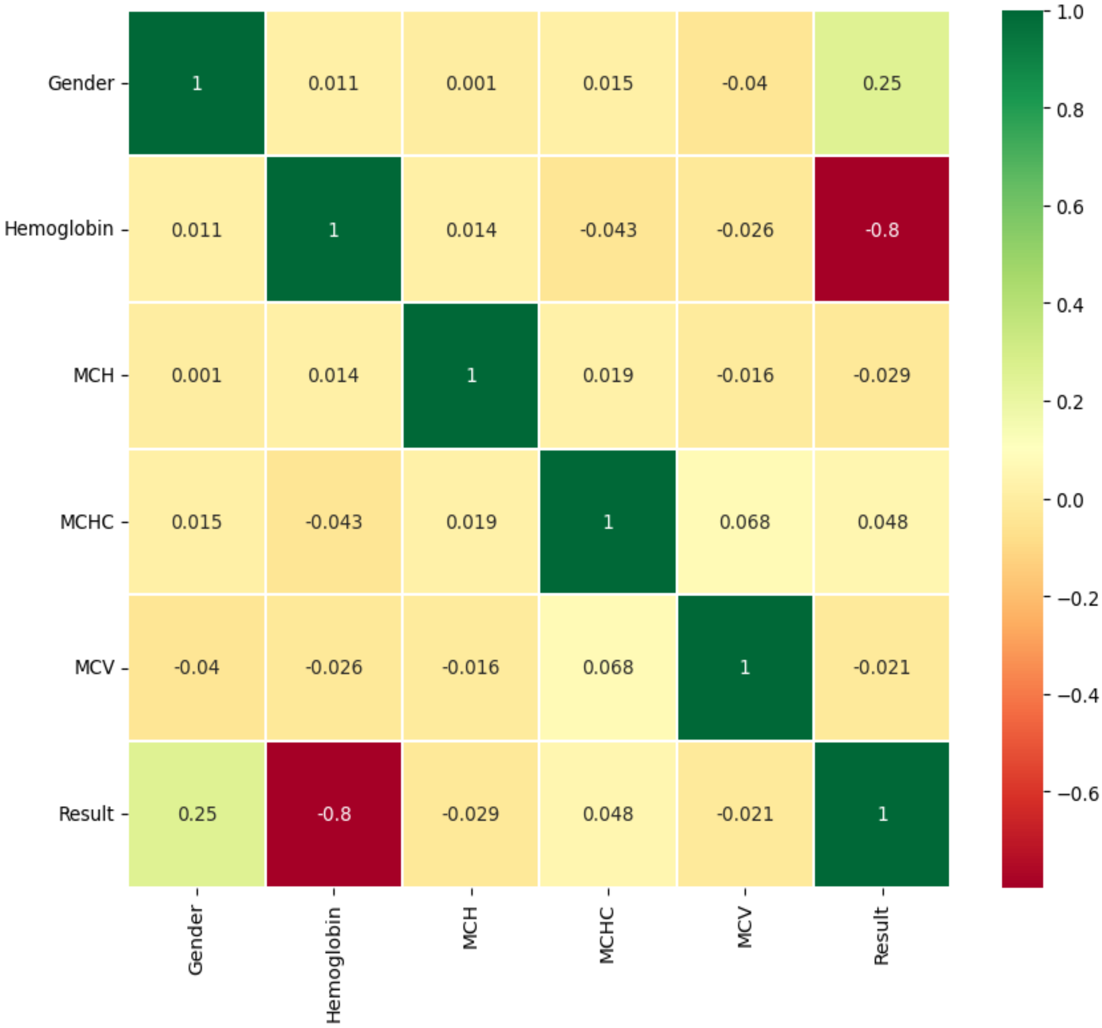

Figure 4. Correlation matrix of indicators of morphological classification of clinical and hematological syndromes

That is, the presence of anemia is mainly determined on the basis of gender and hemoglobin level, and to a lesser extent by other indicators.

To classify the presence of anemia based on blood counts, it does not require the search for complex patterns and a neural network, so we chose logistic regression (as a built-in scikit-learn method). To calculate the final accuracy, cross-validation is used: the data set is divided into five parts, and in turn each of them is used for validation, and the rest for training the model. That is, in each case, 20% of the data is used for verification. The resulting accuracy (5 indicators in total) is averaged, and from here the final accuracy is obtained. In the resulting model, it was 99.1%. Figure 5 shows the error matrix, which indicates that the model falsely named anemia 11 times, and 1 time – did not identify it. In the remaining 1409 cases, the correct diagnosis was established.

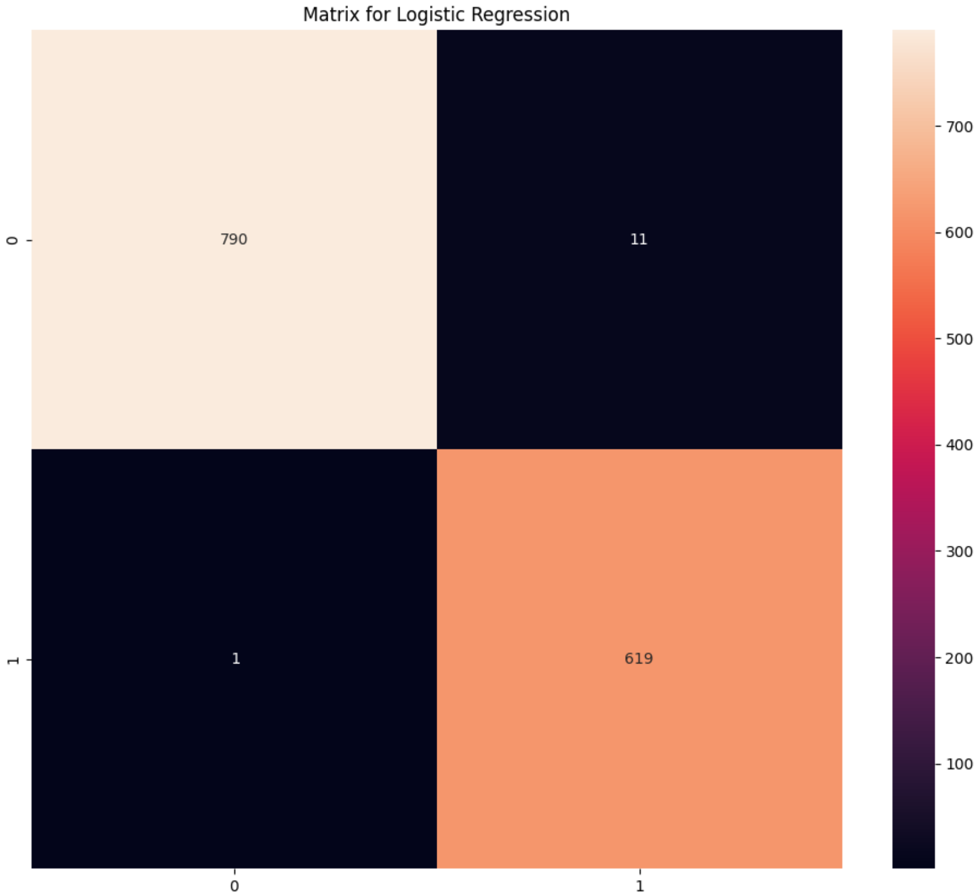

Figure 5. Error Matrix

Conclusion. To date, there is a large volume of hematological medical data collected as a result of medical tests. A lot of research is being done to gain knowledge from this data using data mining techniques. For example, the authors [28] conducted three experiments with the test blood dataset using three classifiers: a decision tree, rule induction, and a naive Bayesian approach. The results showed that the naive Bayes classifier has a greater ability to predict blood disease than the other two classifiers.

Deep machine learning for CDS indicators will improve the efficiency of differential diagnostics and apply it to the development of algorithmic and software for an intelligent system to support clinical decision-making [29].

Thus, machine learning technology is becoming an important tool in the development of new high-tech and personalized approaches to the management and monitoring of CDS [30].

The results of the project can be further used in appropriate tests in medicine, to monitor the condition of patients from risk groups (patients with diabetes, Iron deficiency anemia, Anemia of a chronic disease, cardiovascular diseases, pregnant women, etc.) for the purpose of emergency response of monitoring organizations and timely medical care.

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