


Original Article

# Hematology and Hematopathology Insights Powered by Machine Learning: Shaping the Future of Blood Disorder Management

Rahime Tajvidi Asr<sup>1</sup>, Milad Rahimi<sup>1,2</sup>, Mohammad Hossein Pourasad<sup>3</sup>, Salar Zayer<sup>4</sup>, Mohammadreza Momenzadeh<sup>5</sup>, Mustafa Ghaderzadeh<sup>6\*</sup> 

<sup>1</sup>Health and biomedical informatics Research Centers, Urmia University of Medical Sciences, Urmia, Iran.

<sup>2</sup>Student Research Committee, Urmia University of Medical Sciences, Urmia, Iran.

<sup>3</sup>School of paramedical, Kermanshah University of Medical Sciences, Kermanshah, Iran.

<sup>4</sup>School of Medicine, Urmia University of Medical Sciences, Urmia, West Azerbaijan, Iran.

<sup>5</sup>Department of Artificial Intelligence in Medical Sciences, Smart University of Medical Sciences.

<sup>6</sup>Boukan Faculty of Medical Sciences, Urmia University of Medical Sciences, Urmia, Iran.



Scan and read the  
article online

**Citation** Tajvidi Asr R, Rahimi M, Pourasad MH, Zayer S, Momenzadeh MR, Ghaderzadeh M. Hematology and Hematopathology Insights Powered by Machine Learning: Shaping the Future of Blood Disorder Management. Iran J Blood Cancer. 2024 Dec 30;16(4): 9-19.



## Article info:

Received: 19 Nov 2024

Accepted: 02 Dec 2024

Published: 30 Dec 2024

## Abstract

**Introduction:** The field of hematology faces significant challenges in data analysis, especially in the diagnosis and prediction of diseases. Traditional methods of analysis are often time-consuming, complex, or inadequate to handle the complex nature of blood-related data. This requires the development of advanced techniques for accurate prediction and classification. Artificial Intelligence (AI)-based methods have emerged as a powerful solution that enables more efficient and accurate analysis of hematological data. This study aims to systematically review published research on the use of different artificial intelligence algorithms in the analysis of this field of data.

**Methods:** Using a combination of keywords related to blood data analysis and artificial intelligence, we searched medical and scientific databases to identify relevant articles. A data extraction form was developed to collect relevant information from selected studies based on predefined inclusion and exclusion criteria. The content analysis method was used to analyze the extracted data and the findings were organized in tables and figures to meet the research objectives.

**Results:** After reviewing 7300 studies, 25 full-text studies were selected for final analysis based on their relevance to the research objectives. The findings showed that AI methods, especially deep learning (DL), are widely used to predict and diagnose hematological and Hematopathological diseases. Among the most common algorithms used in ML were XGBoost, which was one of the most important deep learning algorithms, as well as Convolutional Neural Networks (CNN). AI-based models had Accuracy, Specificity, and Sensitivity of 96.6%, 95%, and 96%, respectively.

**Conclusion:** This review shows that AI-based models have the potential to be significantly applied to the analysis of blood data. As artificial intelligence continues to evolve, medical professionals and researchers will have access to powerful ML-based tools to quickly and accurately diagnose.

## Keywords:

Hematology  
Hematopathology  
Machine Learning  
Blood Disorder

## \* Corresponding Author:

Mustafa Ghaderzadeh

**Affiliation:** Boukan Faculty of Medical Sciences, Urmia University of Medical Sciences, Urmia, Iran

**E-mail:** [mustafa.ghaderzadeh@gmail.com](mailto:mustafa.ghaderzadeh@gmail.com)

## 1. INTRODUCTION

Today, the applications of artificial intelligence algorithms in the health care industry, like other industries, are known as an important tool[1]. The use of various artificial intelligence algorithms such as machine learning and deep learning algorithms has been widely used in the field of hematology in the last decade. Hematopathology, the study of diseases affecting the blood, bone marrow, lymph nodes, and other components of the hematopoietic and lymphatic systems, is an important discipline within the broader field of pathology. Accurate and timely diagnosis of hematological disorders is necessary to guide appropriate treatment and management strategies. However, the complexity and heterogeneity of many blood-related diseases pose significant challenges for pathologists in accurately interpreting microscopic findings and making a definitive diagnosis[2]. Due to the wide field of blood diseases and abnormalities related to blood, diagnostic methods of these diseases and morphological analysis, biomarkers and blood test results, artificial intelligence algorithms in the field of hematopathology have been able to face this field with a paradigm shift. Rapid advances in artificial intelligence (AI) and machine learning (ML) have opened new avenues to enhance the capabilities of hematopathologists. Algorithms based on artificial intelligence have shown the potential to enhance and optimize various aspects of hematopathological analysis, from identification of cell morphology to identification of biomarkers and prediction of disease prognosis[3]–[5] By extensive search in databases, we found that no study was found that investigated artificial intelligence in the subfields of hematopathology. Therefore, with the wide application of artificial intelligence in the field of hematopathology, we decided to discuss these applications with a review of a study.

## 2. METHOD

Because this study is done as a systematic review, we considered a way to reach it. Its roadmap is as follows: first, the search strategy is developed, and then the search results are obtained. Then searches will be done based on the strategy and each step of searching and reviewing and selecting related studies will be done based on the PRISMA protocol[6].

### 2.1 Search Strategy

The researchers conducted a comprehensive investigation of electronic databases that publish scientific papers in the

medical and computer fields, focusing on the PubMed, Web of Science (WOS), and Scopus databases. By utilizing the keywords and logical phrases outlined in **Table 1**, they searched for relevant articles published during the period from early November 2017 to late April 2022. However, Google Scholar publications were excluded from the search domain due to their proximity to the research topic.

### 2.2 Quality Evaluation

The researchers conducted a quality assessment of the search process as a critical step in their systematic study, which is as important as other phases such as data extraction and analysis. To guide the quality assessment, we used the QUADAS<sup>1</sup> tool[7], which is the closest fit to the scope of their Systematic Literature Review (SLR). The QUADAS tool comprises seven criteria, with four evaluating the risk of bias and the remaining three focused on applicability-related concerns.

### 2.3 Data Extraction

The data extraction process involved addressing various issues related to the research questions. Each study was initially examined by the first reviewer (M.G.) and then subjected to an expert review by a team (M.R) to identify and correct any potential errors in data extraction. The data extraction form included a list of items with their respective definitions, as presented in **Table 1**. Any discrepancies or differences in the searches were resolved through discussions with an independent author (S.Z.). The elements of the extracted data, including the author's name, country of the research, examined population, applied data, purpose, method, and assessment methods, were all evaluated.

### 2.4 Research Questions

After searching for review articles on the diagnosis of CAD and applying the article search method, we have to ask questions that have not been discussed and answered in these studies. These questions are presented below:

1. In which countries and in which years did researchers use artificial intelligence-based techniques to analyze hematopathology data.
2. What goals were considered by researchers in the field of blood data analysis?
3. What data was used in artificial intelligence models for hematopathology?
4. What artificial intelligence methods and algorithms were used to analyze hematopathology data?

<sup>1</sup> Quality Assessment of Diagnostic Accuracy Studies

**Table 1.** Keywords of search strategy.

| Keywords   | Logical Combination of keyword  |
|--|---|
| Hematology, Hematopathology, flow cytometry, Leukemia, CLL, CML, ALL, AML  | #1 Hematology” OR “Hematopathology” OR “flow cytometry” OR “Leukemia” OR “CLL” OR “CML” OR “ALL” OR “AML”   |
| Machine Learning, Classification, Data Mining, decision tree, neural network, Support Vector Machine, ensemble, Bayesian | #2 “Machine Learning” OR “Classification” OR “Data Mining” OR “Data-Mining” OR “decision tree” OR “Artificial Neural Network” OR “Support Vector Machine” OR “ensemble” OR “Bayesian” |
| Final Search strategy  | #1 AND #2   |

5. How did these models based on artificial intelligence perform in the analysis of hematopathology data?

### 3. RESULTS

In this study, researchers identified 7,300 relevant articles by using valid source search strategies. Then, by carefully examining the abstract and full text of these articles and applying appropriate entry and exit criteria, 25 articles were selected according to the research topic.

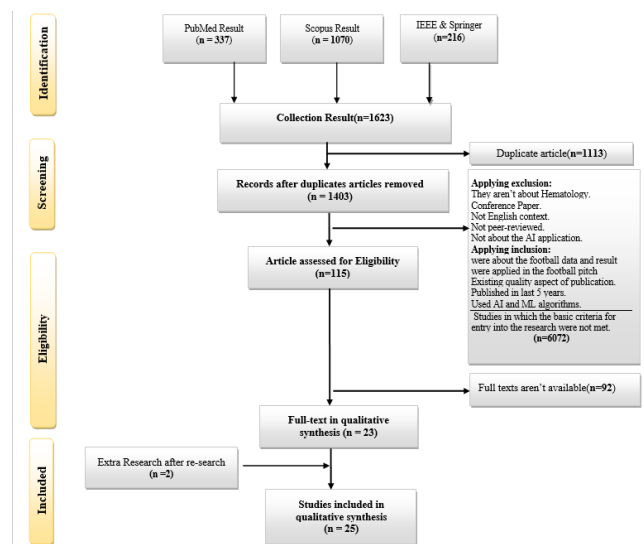
By adopting a systematic and accurate approach, the researchers were able to identify and select relevant and useful articles from among the huge amount of available information. This approach not only helps to increase the credibility and quality of the research, but also provides the possibility of a comprehensive analysis and evaluation of the subject under investigation. In this way, researchers can take steps towards achieving accurate and reliable results. This step-by-step process is depicted in the PRISMA flow diagram of **Figure 1**.

In this text, researchers have reviewed articles related to the use of artificial intelligence and machine learning algorithms to analyze soccer data on the soccer field. The process of this review is as follows:

1. First, the entry and exit criteria of the articles were determined in order to determine the articles related to the present study.
2. Then the abstract of related articles was reviewed.
3. After that, full text of related articles was searched and obtained.
4. Finally, all full-text articles were collected from the databases. These studies included 57 cases that used artificial intelligence and machine learning algorithms to analyze blood and hematopathology data.

#### 3.1 Characteristics of the conducted studies

By reviewing the full text of all the studies conducted in the field of using artificial intelligence and machine learning in



**Figure 1.** PRISMA protocol flowchart of search and exclusion stages.

the field of blood data analysis in the spectrum of hematology and hematopathology measurements, we extracted a table that reflects the main features of these studies. In the current study, the table is extracted and displayed based on items such as the author, the country of the study, the purpose of the study, the data used, the method of the artificial intelligence subset, the algorithms used, the performance of these algorithms, and additional points. In **Table 2**, this main table resulting from the study of this research is displayed.

##### 3.1.1. Geographical features of the conducted studies

The included studies demonstrate a wide geographic distribution, encompassing research conducted in North America, Europe, Asia, and beyond. The majority of studies originate from the United States (n=13), highlighting its significant contribution to the field. Other represented countries include Canada (n=2), Turkey (n=1), the United Kingdom (n=2), Germany (n=2), China (n=2), India (n=1),

**Table 2:** Main table of studies that uses AI methods and algorithms in Hematology diseases and concepts.

| Author's, Country, Years, Reference     | Goals   | Data   | Methods  | Algorithms                           | Performance  | Extra Information  |
|---|---|--|--|--------------------------------------|--|--|
| Bazinet A. et al, 2023,USA [8]          | Automated MRD quantification in CLL using AI-assisted MFC.                      | 113 standard flow cytometry                                    | ML-based analysis compared with expert manual evaluation                 | RF, SVM                              | AI-assisted MRD categorization accuracy: 96%. Pearson's r (AI vs. manual): 0.8650.   | AI-assisted MRD analysis encompassed diverse cases, including unusual immunophenotypes and controls with hematogenous cells, aiming to represent varied clinical scenarios and demonstrating high analytical accuracy based on morphological biomarkers. |
| El Hussein S, et al. USA,2021 [9]       | Enhance CLL diagnostic accuracy using morphologic and architectural biomarkers. | 125 biopsy images (morphological and architectural biomarkers) | ML-driven analysis; statistical validation using t-test and Welch's test | RF                                   | Accuracy and AUC (based on cell size) improved from 0.675 and 0.797 to 0.824 and 0.935, respectively. Improvements also observed in nucleus intensity, cell density, and cell spacing. | AI tools can identify biomarkers in tissue samples to aid in diagnosing aggressive CLL.  |
| Aydin Atasoy N. et al, Turkey,2023 [10] | Improve bone marrow cell classification with CapsNet architectures.             | Bone marrow cell dataset                                       | DL models combined with SMOTE to address class imbalance                 | RES-CapsNet, VGG-CapsNet, GN-CapsNet | Training accuracy: VGG16-CapsNet: 98.95%; RES-CapsNet: 99.24%; GN-CapsNet: 99.45%.   | Combining developed CapsNets with pre-trained models (RES, VGG, GN-) further enhanced performance.   |
| Koga S. et al, USA,2023[11]             | Utilize large language models for medical education and decisions.              | Pathology Outlines question bank                               | Performance comparison of two LLMs (GPT-4 and Google Bard)               | No specific algorithm applied        | Consistency rate: ChatGPT: 85%; Google Bard: 61%.  | ChatGPT achieved higher scores in most subspecialties, while Google Bard excelled in gynecology and digital pathology. Performance varied across medical domains.  |
| Mohlman JS . et al, USA,2020[12]        | Assist hematopathologists in lymphoma differentiation using CNNs.               | 10,818 histologic images                                       | DL-based training with varied parameters and network architectures       | CNN                                  | Best CNN accuracy: 94% (100% accuracy for individual classes). AUC: 0.92 for both DLBCL and BL.  | CNNs show promise in augmenting human expertise for BL/DLBCL differentiation, providing reliable automated image analysis.   |
| Tsakiroglou AM. et al, UK,2023 [13]     | Automate lymphoma diagnosis with AI-based triage system.                        | WSIs of H&E-stained samples                                    | DL-driven automated triage   | CNN                                  | AI triage accuracy: 0.828 ± 0.041. Overall accuracy: 0.932 ± 0.024.  | AI-based automated triage offers potential for timely and accurate lymphoma diagnosis, improving patient care.   |
| Sasaki K. et al. USA, 2021[14]          | Predict optimal TKI treatment for CML to improve survival.                      | 630 patient characteristics                                    | ML analysis to optimize survival outcomes                                | XGBoost DT                           | AUC in the test cohort: 0.819.   | The LEAP model uses a boosting decision tree method for optimal TKI recommendations. Age, comorbidities, and LEAP-recommended therapy were identified as independent prognostic factors.   |
| Fazeli S. et al ,USA,2021 [15]          | Improve bone marrow morphology recognition with deep learning.                  | 71,374 images from 945 patients                                | DL and ML integration using self-supervised models                       | DNN, ResNet-50                       | Macro-average precision increased by 0.07 and 0.04 compared to baseline. Macro-average F1 score increased by 0.07 compared to baseline.  | Significant performance improvement was observed compared to existing methods, with optimal results from an unsupervised approach.   |
| Osman M. et al, USA, 2021 [16]          | Classify monocytes and related cells for hematological malignancy diagnostics.  | 935 digital images of monocytic cells.                         | DL classification framework  | CNN                                  | CNN accuracy comparable to human reviewers (0.78 ± 0.10 vs. 0.86 ± 0.05).  | This study is the first to attempt separating monocytes from their precursors using CNNs.  |

|   |  |  |  |  |   |  |
|---|--|--|--|--|---|--|
| Lu Z. et al, USA,2021[17]               | Validate DeepFlow™ AI for lymphocyte subset classification efficiency.         | 379 clinical flow cytometry cases.                                   | ML-driven comparison of manual and automated workflows                             | T-SNE, K-means, Rule-Based Analysis              | Strong correlation ( $r > 0.9$ ) observed across lymphocyte subsets.  | AI-assisted flow cytometry demonstrates accuracy and efficiency, providing a transformative diagnostic approach.   |
| Hasan E. et al, USA, 2021[18]           | Compare MCS and SBA for accurate white blood cell diagnosis.                   | WBC images   | ML and DL algorithms for comparative performance analysis                          | KNN, GoogLeNet (with transfer learning)          | Accuracy: 94%.  | Similarity-based algorithms improved novice but not expert performance.  |
| Mu Y. et al, Canada,2023 [19]           | Optimize bone marrow WSI analysis using multiple instance learning.            | 556 cytology slides  | DL methods combined with multiple instance learning                                | KNN, YOLO  | Mean Average Precision at 10 (mAP@10): $0.58 \pm 0.02$ (vs. random retrieval baseline of $0.39 \pm 0.1$ ). Weighted-average F1 score for diagnostic labels: $0.57 \pm 0.03$ . | This method can summarize complex semantic information in WSIs, potentially supporting AI-assisted computational pathology.  |
| Saxena S. et al ,India,2023[20]         | Detect malaria parasites in blood smears using deep learning.                  | 352 Leishman–Giemsa-stained peripheral blood images                  | DL optimization of sensitivity and specificity                                     | DCNN, Inception V3                               | Model D: Sensitivity: 85%; Specificity: 94%.  | This study is an initial step toward automated malaria parasite screening, emphasizing potential improvements in diagnostic efficiency and accuracy.                       |
| Zhang Z. et al, China,2022 [21]         | Enhance CML diagnosis with cGAN-based bone marrow segmentation.                | 517 bone marrow biopsies   | DL with cGAN for segmentation  | cGAN   | Mean pixel accuracy: 0.95. Mean Intersection over Union (IoU): 0.71. Mean Dice coefficient: 0.81. Best AUC: 0.84.   | cGAN outperformed other models, using segmented cell features for robust clinical prediction, validated via cross-validation.  |
| Abele N. et al, Germany,2023 [22]       | Evaluate AI for Ki-67 and hormone receptor quantification in breast cancer.    | 204 slides (72 Ki-67, 66 ER, and 66 PR)                              | DL for quantification and comparison with pathologist manual scoring               | CNN  | Ki-67 accuracy: 0.95. ER/PR accuracy: 0.93.   | The AI tool improved interobserver reliability in marker scoring across diverse conditions, highlighting the need for real-world validation.                               |
| Raju GS. et al, USA,2015[23]            | Extract adenoma detection rate from colonoscopy reports with NLP.              | 12,748 patient colonoscopy records                                   | NLP to extract adenoma detection rate  | NLP  | NLP correctly identified 91.3% of screening examinations, compared to 87.8% by manual method.   | NLP offers a more efficient approach for calculating real-time quality metrics, with potential for clinical integration.   |
| Mu Y. et al, Canada,2024 [24]           | Improve WSI quality by excluding irrelevant patches for better classification. | 717 de-identified bone marrow trephine biopsy WSIs from 616 patients | DL with binary patch grouping to enhance classification                            | CNN  | mAP@10: 0.506. Weighted-F1: 0.475.  | BPG optimizes patch grouping, addressing variability and time consumption in histopathology, improving computational pathology applications.                               |
| Wang C-W.et al, Taiwan,2022 [25]        | Analyze bone marrow differential counts using hierarchical deep learning.      | Train dataset: 12,426, Test dataset: 3,005                           | Automated cell identification and classification using hierarchical deep learning. | Automatic Hierarchical Deep Learning Framework.  | Recall: 0.84. Accuracy: 0.98.   | Achieves BM NDC analysis in 44 seconds, using WSIs with 40x magnification, and is the first study to demonstrate automatic BM NDC with such high efficiency.               |
| Brinker TJ, et al, Germany,2021 [26]    | Predict melanoma lymph node metastasis from H&E slides using AI.               | 15 H&E slides from primary melanoma tumors.                          | ML-based prediction from H&E-stained slides  | ANNs   | Accuracy: 0.61. AUROC: 0.55.  | Current Acc is not clinically relevant, highlighting the need for larger datasets to improve predictive performance.   |
| Sirinukunwattana K, et al, UK 2020 [27] | Identify megakaryocyte features to improve MPN diagnosis and subtyping.        | 62,479 annotated megakaryocyte cells.                                | ML and DL for megakaryocyte identification and analysis                            | Autoencoder Neural Network, Single Shot Multibox | AUC: 0.95.  | The approach enhances diagnostic Acc, provides visual representation of features, and supports routine diagnostics, disease monitoring, and treatment response assessment. |

|   |  |   |  | Detector (SSD), U-Net               |  |  |
|---|--|---|--|-------------------------------------|--|--|
| El Hussein S .et al,USA 2022 [26]         | Delineate proliferation centers in CLL biopsies using AI-based tools.      | 74 ROIs from 30 CLL, aCLL, and RT cases using H&E-stained slides. | DL for distinguishing proliferation centers and subtypes.  | CNN                                 | Accuracy: 0.81. AUC: 0.88.   | This AI-based method offers an automated and objective way to distinguish CLL, aCLL, and RT, particularly useful in small needle biopsy specimens.   |
| Yenamandra AK.et al,USA,2021 [28]         | Classify high-risk plasma cell myeloma using ANN and SVM models.           | 477 PCM cases   | ML models to classify high-risk categories at diagnosis  | ANN, SVM                            | ANN accuracy: 94%; Precision: 0.97; Recall: 0.76. LR accuracy: 1.0. SVM accuracy: 95% (for plasma cells vs. TP53). | The ANN model identified associations between WBC count, BM plasma cell percentage, and high-risk genetic categories in PCM.   |
| Su J.et al, China, 2017[29]               | Segment bone marrow aspirate images for better AML diagnosis.              | 1,200 BMA cell samples  | DL-based segmentation for blast cell identification  | K-means clustering, HMRF            | Accuracy: 0.97.  | The method assists in differentiating six cell groups and enhances the Acc of blast counting, offering a more efficient and reliable approach for AML diagnosis.   |
| Xu-Monette ZY.et al, USA, 2020[30]        | Refine COO classification in DLBCL using AI and RNA sequencing.            | 418 DLBCL cases incorporating genetic and transcriptional data.   | Integration of genetic and RNA sequencing data with AI for COO assignment and clinical prediction. | NGS-COO Classifier, Survival Models | AUC: 0.96.   | The study demonstrated that AI deep learning applied to targeted RNA-Seq provides efficient, reproducible, and cost-effective assays, aligning with WHO classification standards and supporting precision medicine in DLBCL. |
| Acevedo A.et al, Spain,2021 [3], [8]-[31] | Recognize hypogranulated neutrophils for MDS diagnosis using DysplasiaNet. | 20,670 hypogranulated neutrophils images.                         | DL for objective recognition of neutrophil morphology  | CNN                                 | Sensitivity: 95.5%; Specificity: 94.3%; Precision: 94%; Accuracy: 94.85%.  | The DysplasiaNet model is designed to reduce inter-observer variability and integrate seamlessly into clinical laboratory workflows for MDS diagnosis.   |

Taiwan (n=1), and Spain (n=1). In terms of publication years, most studies were published between 2020 and 2023, reflecting recent advancements and ongoing interest in the area of study. Notably, the earliest included study dates back to 2015, while the most recent study is from 2024, underscoring the relevance of this research over nearly a decade. This temporal spread indicates a sustained and growing academic focus across diverse geographic regions.

### 3.1.2. Overview of the studies Goals

The studies targeting hematological malignancies demonstrate significant advancements in both diagnostic accuracy and workflow efficiency. Bazinet et al. (2023, USA) and El Hussein et al. (2021, USA) focused on improving chronic lymphocytic leukemia (CLL) diagnostics. Bazinet et al. developed AI-assisted multiparametric flow cytometry (MFC) for automated minimal residual disease (MRD) quantification, while El Hussein et al. utilized morphological and architectural biomarkers to enhance diagnostic precision. Similarly, Osman et al. (2021, USA) aimed to classify monocytes and related cells to aid hematological malignancy diagnostics, and Fazeli et al. (2021, USA) applied deep learning to enhance bone marrow morphology recognition. These efforts collectively address the challenges of heterogeneity and complexity in hematological diagnostics, providing reliable and efficient tools for clinical implementation. In lymphoma differentiation, Mohlman et al. (2020, USA) employed convolutional neural networks (CNNs) to support hematopathologists, while Tsakiroglou et al. (2023, UK) automated lymphoma diagnosis through an AI-based triage system, streamlining workflows and improving patient outcomes.

In terms of advancing bone marrow and cellular analysis, studies explored both novel architectures and automated systems. Aydin Atasoy et al. (2023, Turkey) and Wang et al. (2022, Taiwan) applied hierarchical deep learning and CapsNet architectures to improve bone marrow cell classification and differential counts. Su et al. (2017, China) and Zhang et al. (2022, China) focused on segmentation methods, using advanced deep learning models like conditional GANs to refine bone marrow aspirate images and enhance CML diagnosis. Lu et al. (2021, USA) validated DeepFlow™ AI for efficient lymphocyte subset classification, while Hasan et al. (2021, USA) compared manual counting systems (MCS) with semi-automated approaches (SBA) to improve white blood cell diagnostics. The integration of AI into bone marrow WSI analysis was exemplified by Mu et al. (2023, 2024, Canada), optimizing

image quality and excluding irrelevant patches to achieve better diagnostic precision.

In cancer diagnosis and pathology, several studies demonstrated the transformative potential of AI. Brinker et al. (2021, Germany) predicted melanoma lymph node metastasis using H&E slides and AI, while Abele et al. (2023, Germany) evaluated AI for quantifying Ki-67 and hormone receptors in breast cancer. Acevedo et al. (2021, Spain) developed Dysplasia Net to identify hypogranulated neutrophils for myelodysplastic syndrome (MDS) diagnosis, and Sirinukunwattana et al. (2020, UK) utilized AI to assess megakaryocyte features for improving myeloproliferative neoplasm (MPN) diagnosis. Yenamandra et al. (2021, USA) and Xu-Monette et al. (2020, USA) applied artificial neural networks (ANNs) and RNA sequencing to classify high-risk plasma cell myeloma and refine cell-of-origin classification in diffuse large B-cell lymphoma (DLBCL), respectively. These studies collectively underscore the potential of AI to enhance diagnostic consistency, improve prognostic assessments, and support precision medicine in diverse clinical scenarios[11].

### 3.1.3. Used Data in Studies used AI in Homologies analysis Data

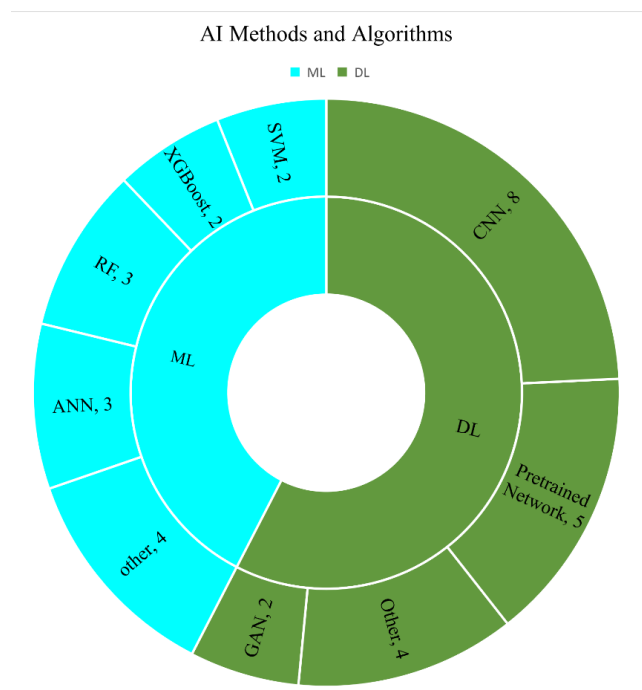
The datasets utilized in the reviewed studies were diverse and categorized by data types and diseases. Imaging datasets included 71,374 bone marrow morphology images (et al., USA, 2021), 10,818 histologic images (Mohlman et al., USA, 2020), and 352 Leishman-Giemsa-stained peripheral blood images (Saxena et al., India, 2023)[14] [19][12], [13]. Whole-slide images (WSIs) of H&E-stained samples were used for lymphoma (Tsakiroglou et al., UK, 2023) and bone marrow biopsy classification (Mu et al., Canada, 2024), while hypogranulated neutrophils were identified from 20,670 images for MDS diagnosis (Acevedo et al., Spain, 2021). Flow cytometry datasets included 113 standard cases for CLL (et al., USA, 2023) and 379 clinical cases for lymphocyte subset classification (Lu et al., USA, 2021). For patient-level datasets, 630 patient characteristics were analyzed for TKI treatment prediction in CML (Sasaki et al., USA, 2021), and 418 DLBCL cases incorporated genetic and transcriptional data (Xu-Monette et al., USA, 2020) [12], [13] These datasets were critical for developing AI models across hematological, oncological, and diagnostic applications, enabling robust training and validation of methodologies.

### 3.1.4. AI Methods and Algorithms in the Analysis of Hematological Data

In general, the methods of artificial intelligence used in the field of data analysis of blood diseases, three main methods

of artificial intelligence have been used. As the artificial intelligence methods have three methods: machine learning, deep learning and productive intelligence, the researchers used these artificial intelligence methods and the algorithms of these methods. The methods used can be determined from the type of data used and the dataset under investigation. There was no special method in choosing the algorithms of these methods, but based on previous studies or trial and error. In the **Figure 2** all the used models and algorithms of these methods have been done with multiple goals.

This chart comprehensively displays the types of artificial intelligence methods used in the prediction and diagnosis of blood diseases in hematology and hematopathology data in studies. The ML (Machine Learning) section includes methods such as XGBoost.2, RE.3 and ANN.3 (Layered Artificial Neural Network), while the DL method includes CNN (Neural Network) and Pretrained Network.5 algorithms. Various methods have been used to analyze blood data, and this diversity in the use of artificial intelligence methods shows that researchers can solve complex problems from a wide range of Algorithms are used and by choosing appropriate methods for each specific problem, they achieve more optimal results. This can lead to the increasing progress of artificial intelligence applications in various fields.



**Figure 2.** Methods and Algorithms used to classification hematology data.

### 3.1.5. The performance of AI models in the analysis of hematology and hematopathology data

Various metric has been proposed to evaluate the performance of models based on machine learning and deep learning, which depend on the purpose of the study as well as the ideology of the researcher, but in general, these criteria have generalities that these criteria are widely used. Overall, the most important text discussed here is on common performance metrics used in artificial intelligence models used in soccer data analysis. One of the most widely used performance measures, especially for detection and classification, is accuracy. This metric shows the ratio of accurate model predictions to total predictions. Although accuracy is a simple and understandable measure, it can be misleading when class differences exist. In this situation, alternative measures such as accuracy, recovery, and F1 score may provide a more unbiased assessment of model performance. But in order to measure the performance of the models in the correct diagnosis of diseases and abnormalities, they used the sensitivity scale. In addition to these indicators, a specific metric can be used to detect the absence of disease or abnormality, and the researchers used it.

One of the common measures for regression problems is the mean squared error. The mean squared difference between the actual target values and the predicted values is measured by this metric. Because high errors are given more weight, MSE is sensitive to outliers. Better model performance is indicated by lower MSE, so the whole model has zero MSE. The F1 score provides a fair assessment of model performance because it is the geometric mean of precision and recovery. This scale, which goes from 0 to 1, indicates perfect accuracy and recovery. The F1 score is particularly useful when working with unbalanced data sets, when accuracy may not be a valid measure by itself.

Mean absolute error (MAE) is another regression measure that measures the average absolute value of the difference between the predicted and actual values. Unlike MSE, MAE is not more sensitive to outlier observations, it is more resistant to it. A lower MAE indicates a better model performance, so that the full model has zero MAE.

These performance metrics provide complementary insight into model behavior and are typically used in combination to comprehensively understand a model's strengths and weaknesses. The choice of criterion(s) depends on the specific objectives of the research, the problem domain, and the characteristics of the case data.

It has an analysis. After reviewing the studies and calculating the performance criteria of the models, it is possible to

realize the high performance of this research and the acceptability of the results for researchers. Almost all studies have acknowledged the success of artificial intelligence methods and machine learning and deep learning algorithms and calculated related metrics based on the performance of these models. In these studies, the average amount of these metrics has been calculated in the **Table 3**. After calculating the average performance criteria of different artificial intelligence models used in the analysis of data related to hematological diseases, it can be concluded that the overall performance of these models has reached an acceptable and satisfactory level from the point of view of clinical experts. These models have demonstrated the ability to provide reliable and accurate insights that can potentially assist healthcare professionals in the diagnosis, prognosis, and management of blood-related disorders. The improved performance of these AI systems, achieved through advances in algorithms and training techniques, demonstrates the growing potential of using machine learning and deep learning approaches to enhance clinical decision making in the field of hematology. As these AI-based tools continue to evolve and integrate seamlessly with medical workflows, they are poised to become valuable assets in improving patient outcomes and streamlining healthcare delivery in the area of hematologic disease management.

**Table 3.** The average performance metrics of the conducted studies

| Metric | Accuracy | Specificity | Sensitivity | AUC          |
|--------|----------|-------------|-------------|--------------|
| Value  | 96%      | 95%         | 96.6%       | <b>96.5%</b> |

#### 4. DISCUSSION AND FURTHER RECOMMENDATIONS

In recent years, experts and researchers have shown increasing interest in the application of deep learning (DL) techniques in the analysis of blood data and hematological diseases. Over the past five years, these methods have been widely used for tasks such as disease diagnosis, prognosis prediction, and treatment optimization. The present study developed a comprehensive search strategy, identified 25 relevant studies, and performed an in-depth analysis of research focusing on the application of artificial intelligence (AI) techniques in hematology. To answer the research questions, the selected studies were evaluated based on the key indicators listed in the initial table of the study. The analysis found that nearly all of the studies were conducted in the past five years, and reflects the growing interest of the medical community and researchers in finding more accurate, collaborative, and effective ways to analyze blood-related data. It was observed that the goal of medical researchers is not to replace human expertise with

artificial intelligence, but rather they see artificial intelligence-based tools as complementary assistants to the knowledge of hematologists and medical specialists. The selection of AI algorithms in these studies was mainly based on data, and the researchers selected the most optimal algorithms based on their performance. The data used in these studies were mostly retrospective and relied on pooled data sets.

In almost all cases where artificial intelligence algorithms were used, the performance of these models was considered acceptable by medical experts and doctors. Researchers have consistently confirmed the superior performance of AI models compared to traditional diagnostic methods. However, as the use of intelligent models based on machine learning (ML) and deep learning (DL) techniques continues to grow, especially in areas such as early disease diagnosis and personalized treatment planning, several issues should be addressed in future research. be noticed the following gaps were identified:

The identified gaps – data preprocessing, data sufficiency and prevention of overfitting – are particularly relevant in the context of blood data and hematological diseases. For example:

**Data preprocessing:** In hematology, raw data from blood tests, genetic analyses, or imaging often require extensive preprocessing, including normalization, outlier removal, and feature extraction, to ensure accurate model training.

**Sufficient data:** large data sets are critical for identifying patterns in blood-related diseases, such as anemia, leukemia, or coagulation disorders. Insufficient data can lead to unreliable models, especially in rare diseases where data deficiency is a common issue.

**Avoiding overfitting:** Overfitting is an important concern in medical research, where models trained on limited data sets may fail to generalize to new patient populations. Techniques such as regularization, data augmentation, and ensemble methods can help reduce this risk.

Consequently, while the study focused primarily on blood data and hematological diseases, the gaps identified—data preprocessing, data sufficiency, and prevention of overfitting—are universally applicable in many contexts, including medical research. Addressing these challenges will be necessary to advance the use of artificial intelligence and ML techniques in hematology and improve patient outcomes.

#### 5. CONCLUSION

With the development of artificial intelligence methods such as machine learning (ML) and deep learning (DL), models based on these techniques are becoming an integral

part of hematology diagnostics and treatment strategies. The use of these tools paves the way to provide expert insights and recommendations to hematologists and medical professionals in areas such as disease diagnosis, prognosis prediction and treatment optimization. As a tool in the hands of healthcare providers, these models, implemented as software modules, can help prevent diagnostic errors, optimize treatment plans, and provide real-time data to enhance clinical decision-making. do Even DL-based systems can be used to design mobile applications for patients in the future. Additionally, such tools can improve patient engagement and understanding by providing personalized health alerts, treatment summaries, and educational resources.

After reviewing multiple methods in hematology using machine learning, it is suggested that future studies combine clinical data, genetic information, imaging data, and other metadata for faster and more accurate insights. It is also recommended that the capabilities of pre-trained neural networks be explored in future research to utilize existing knowledge and improve model performance. In countries with strong medical data repositories, these datasets can be used with machine learning algorithms to revolutionize the way hematological diseases are diagnosed, monitored and treated. This approach has the potential to significantly improve patient outcomes and advance the field of hematology. With the development of artificial intelligence methods such as machine learning (ML) and deep learning (DL), models based on these techniques have become an integral part. They are converted from hematology diagnoses and treatment strategies. The use of these tools paves the way to provide expert insights and recommendations to hematologists and medical professionals in areas such as disease diagnosis, prognosis prediction and treatment optimization. As a tool in the hands of healthcare providers, these models, implemented as software modules, can help prevent diagnostic errors, optimize treatment plans, and provide real-time data to enhance clinical decision-making. do Even DL-based systems can be used to design mobile applications for patients in the future. Additionally, such tools can improve patient engagement and understanding by providing personalized health alerts, treatment summaries, and educational resources.

After reviewing multiple methods in hematology using machine learning, it is suggested that future studies combine clinical data, genetic information, imaging data, and other metadata for faster and more accurate insights. It is also recommended that the capabilities of pre-trained neural networks be explored in future research to utilize existing knowledge and improve model performance. In countries

with strong medical data repositories, these datasets can be used with machine learning algorithms to revolutionize the way hematological diseases are diagnosed, monitored and treated. This approach has the potential to significantly improve patient outcomes and advance the field of hematology.

### Acknowledgment

I would like to formally express my deepest gratitude and appreciation to all the anonymous reviewers of this manuscript, as well as to Dr. Davood Bashash, for their invaluable contributions that made this research possible

### Conflict of interest

All authors declare that there is no conflict of interest.

### References

1. M. Ghaderzadeh, A. Shalchian, G. Irajian, H. Sadeghsalehi, and B. Sabet, "Artificial intelligence in drug discovery and development against antimicrobial resistance: A narrative review," *Iran. J. Med. Microbiol.*, vol. 18, no. 3, pp. 135–147, 2024.
2. M. Ghaderzadeh, M. Aria, A. Hosseini, F. Asadi, D. Bashash, and H. Abolghasemi, "A fast and efficient CNN model for B-ALL diagnosis and its subtypes classification using peripheral blood smear images," *Int. J. Intell. Syst.*, vol. 37, no. 8, pp. 5113–5133, 2022.
3. A. Bazinet et al., "Automated quantification of measurable residual disease in chronic lymphocytic leukemia using an artificial intelligence-assisted workflow," *Cytom. Part B Clin. Cytom.*, vol. 106, no. 4, pp. 264–271, 2024.
4. T. Dehkharghanian, Y. Mu, H. R. Tizhoosh, and C. J. V Campbell, "Applied machine learning in hematopathology," *Int. J. Lab. Hematol.*, vol. 45, no. S2, pp. 87–94, 2023.
5. Y. Hu, Y. Luo, G. Tang, Y. Huang, J. Kang, and D. Wang, "Artificial intelligence and its applications in digital hematopathology," *Blood Sci.*, vol. 4, no. 3, pp. 136–142, 2022.
6. D. Moher et al., "Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement," *Syst. Rev.*, vol. 4, pp. 1–9, 2015.
7. P. F. Whiting et al., "QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies," *Ann. Intern. Med.*, vol. 155, no. 8, pp. 529–536, 2011.
8. S. El Hussein, P. Chen, L. J. Medeiros, J. D. Hazle, J. Wu, and J. D. Khoury, "Artificial intelligence-assisted mapping of proliferation centers allows the distinction of accelerated phase from large cell transformation in chronic lymphocytic leukemia," *Mod. Pathol.*, vol. 35, no. 8, pp. 1121–1125, 2022.
9. N. Aydin Atasoy and A. Faris Abdulla Al Rahhawi, "Examining the classification performance of pre-trained capsule networks on imbalanced bone marrow cell dataset," *Int. J. Imaging Syst. Technol.*, vol. 34, no. 3, p. e23067, May 2024.
10. S. Koga, "Exploring the pitfalls of large language models: Inconsistency and inaccuracy in answering pathology board

examination-style questions," *Pathol. Int.*, vol. 73, no. 12, pp. 618–620, Dec. 2023.

11. J. S. Mohlman, S. D. Leventhal, T. Hansen, J. Kohan, V. Pascucci, and M. E. Salama, "Improving Augmented Human Intelligence to Distinguish Burkitt Lymphoma from Diffuse Large B-Cell Lymphoma Cases," *Am. J. Clin. Pathol.*, vol. 153, no. 6, pp. 743–759, 2020.

12. A. M. Tsakiroglou et al., "Lymphoma triage from H&E using AI for improved clinical management," *J. Clin. Pathol.*, vol. 78, no. 1, pp. 28–33, 2025.

13. K. Sasaki et al., "The LEukemia Artificial Intelligence Program (LEAP) in chronic myeloid leukemia in chronic phase: A model to improve patient outcomes," *Am. J. Hematol.*, vol. 96, no. 2, pp. 241–250, 2021.

14. S. Fazeli, A. Samiei, T. D. Lee, and M. Sarrafzadeh, "Beyond Labels: Visual Representations for Bone Marrow Cell Morphology Recognition," in *Proceedings - 2023 IEEE 11th International Conference on Healthcare Informatics, ICHI 2023*, 2023, pp. 111–117.

15. M. Osman et al., "Classification of monocytes, promonocytes and monoblasts using deep neural network models: An area of unmet need in diagnostic hematopathology," *J. Clin. Med.*, vol. 10, no. 11, 2021.

16. Z. Lu et al., "Validation of Artificial Intelligence (AI)-Assisted Flow Cytometry Analysis for Immunological Disorders," *Diagnosics*, vol. 14, no. 4, 2024.

17. E. Hasan, Q. Eichbaum, A. C. Seegmiller, C. Stratton, and J. S. Trueblood, "Improving Medical Image Decision-Making by Leveraging Metacognitive Processes and Representational Similarity," *Top. Cogn. Sci.*, vol. 14, no. 2, pp. 400–413, Apr. 2022.

18. Y. Mu, H. R. Tizhoosh, T. Dehkharghanian, and C. J. V Campbell, "Whole slide image representation in bone marrow cytology," *Comput. Biol. Med.*, vol. 166, p. 107530, 2023.

19. S. Saxena, P. Sanyal, M. Bajpai, R. Prakash, and S. Kumar, "Trials and tribulations: Developing an artificial intelligence for screening malaria parasite from peripheral blood smears," *Med. J. Armed Forces India*, 2023.

20. Z. Zhang et al., "The Diagnosis of Chronic Myeloid Leukemia with Deep Adversarial Learning," *Am. J. Pathol.*, vol. 192, no. 7, pp. 1083–1091, 2022.

21. N. Abele et al., "Noninferiority of Artificial Intelligence-Assisted Analysis of Ki-67 and Estrogen/Progesterone Receptor in

Breast Cancer Routine Diagnostics," *Mod. Pathol.*, vol. 36, no. 3, p. 100033, 2023.

22. G. S. Raju et al., "Natural language processing as an alternative to manual reporting of colonoscopy quality metrics," *Gastrointest. Endosc.*, vol. 82, no. 3, pp. 512–519, 2015.

23. Y. Mu, H. R. Tizhoosh, T. Dehkharghanian, S. Alfasly, and C. J. V Campbell, "Model-Agnostic Binary Patch Grouping for Bone Marrow Whole Slide Image Representation," *Am. J. Pathol.*, vol. 194, no. 5, pp. 721–734, 2024.

24. C.-W. Wang, S.-C. Huang, Y.-C. Lee, Y.-J. Shen, S.-I. Meng, and J. L. Gaol, "Deep learning for bone marrow cell detection and classification on whole-slide images," *Med. Image Anal.*, vol. 75, p. 102270, 2022.

25. T. J. Brinker et al., "Deep learning approach to predict sentinel lymph node status directly from routine histology of primary melanoma tumours," *Eur. J. Cancer*, vol. 154, pp. 227–234, 2021.

26. K. Sirinukunwattana et al., "Artificial intelligence-based morphological fingerprinting of megakaryocytes: a new tool for assessing disease in MPN patients," *Blood Adv.*, vol. 4, no. 14, pp. 3284–3294, 2020.

27. S. El Hussein et al., "Artificial intelligence strategy integrating morphologic and architectural biomarkers provides robust diagnostic accuracy for disease progression in chronic lymphocytic leukemia," *J. Pathol.*, vol. 256, no. 1, pp. 4–14, Jan. 2022.

28. J. Su, S. Liu, and J. Song, "A segmentation method based on HMRF for the aided diagnosis of acute myeloid leukemia," *Comput. Methods Programs Biomed.*, vol. 152, pp. 115–123, 2017.

29. Z. Y. Xu-Monette et al., "A refined cell-of-origin classifier with targeted NGS and artificial intelligence shows robust predictive value in DLBCL," *Blood Adv.*, vol. 4, no. 14, pp. 3391–3404, 2020.

30. A. Acevedo, A. Merino, L. Boldú, Á. Molina, S. Alférez, and J. Rodellar, "A new convolutional neural network predictive model for the automatic recognition of hypogranulated neutrophils in myelodysplastic syndromes," *Comput. Biol. Med.*, vol. 134, p. 104479, 2021.

31. A. K. Yenamandra, C. Hughes, and A. S. Maris, "Artificial Intelligence in Plasma Cell Myeloma: Neural Networks and Support Vector Machines in the Classification of Plasma Cell Myeloma Data at Diagnosis," *J. Pathol. Inform.*, vol. 12, no. 1, p. 35, 2021.