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A Review on White Blood Cell Classification for Leukemia Diagnosis Using Deep and Transfer Learning Techniques

Dilan Thamir Abdullah[1], Adnan Mohsin Abdulazeez[2]
delanthamer10@gmail.com[1], adnan.mohsin@dpu.edu.krd[2]
[1] Akre University for Applied Science/Technical College of Informatic-Akre/Department of Information Technology-Kurdistan Region- Iraq
[2] Technical College of Engineering, Duhok Polytechnic University, Duhok, Iraq

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Abstract

Leukemia is a severe hematological malignancy that disrupts normal blood cell function, primarily affecting white blood cells (WBCs). Early and accurate Classification of white blood cells (WBCs) is essential for facilitating the accurate diagnosis of leukemia, thereby improving patient outcomes and reducing treatment costs. This paper provides a comprehensive review of recent deep learning and transfer learning approaches applied to WBC classification and leukemia diagnosis. Various models, including Convolutional Neural Networks (CNNs), Vision Transformers (ViT), and hybrid techniques combining handcrafted and learned features, are examined. Performance metrics such as accuracy, sensitivity, specificity, and F1-score are discussed across multiple datasets like BCCD, ALL-IDB, and Kaggle repositories. The study highlights the strengths of different models, addresses challenges such as class imbalance and data scarcity, and outlines future directions like the integration of multimodal data and real-time deployment. This review serves as a valuable resource for researchers and clinicians aiming to develop intelligent, automated systems for hematological disease diagnosis.

A. Introduction

Leukemia is a form of cancer that originates in the blood and bone marrow [1]. It poses a significant health risk, particularly to children under the age of 15 and adults over 55 [2]. The disease is divided into four primary types: acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML) [3]. And it occurs when there is an unnecessary production of immature white blood cells of a kind called blast cells in the bone marrow and the blood that interfere with the regular activity of other healthy blood cells Creating a decrease in the amount of healthy blood cells in the body. [4]. The exact causes of leukemia remain unclear, despite the fact that it has been connected to genetic alterations, chemical exposures, radiation, and viral infections. Managing leukemia presents various challenges, including chronic fatigue, bruising, and weight loss [5]. In 2021, an estimated 1,898,160 people in the United States were expected to be affected by leukemia, with around 186,400 new diagnoses and 57,750 deaths. Leukemia was projected to account for 9.5% of all cancer-related deaths [6]. In 2022, this figure rose to approximately 1,918,030 new cases and some 609,360 related deaths [7]. As such, the early detection of immature blood cells is essential for improving the survival of leukemia. Early and precise diagnosis not only increases the chances of cure but also assists in reducing treatment costs [8]. Blood is primarily composed of three major elements: white blood cells (WBCs), red blood cells (RBCs), and platelets [9]. In individuals affected by leukemia, there is often a reduction in RBCs and platelets, while WBC counts rise due to the abnormal presence of immature leukemic cells [7]. WBCs are categorized into two major groups based on the presence of cytoplasmic granules: granulocytes and agranulocytes. Granulocytes include neutrophils and eosinophils, whereas agranulocytes consist of lymphocytes and monocytes. Each category exhibits unique structural characteristics, such as nuclear morphology and cytoplasmic appearance, that assist in microscopic identification. Despite their importance, manual WBC analysis is labor-intensive and subject to human error. Fortunately, advances in computer-aided diagnostic tools have enabled the precise and automated classification of WBCs through machine learning and image recognition models [10]. In healthy individuals, normal WBC counts are typically. Leukocytosis is defined as a WBC count exceeding 11,000 cells per cubic millimeter [11]. Microscopic examination of white blood cells (WBCs) in blood or bone marrow samples is crucial for early disease detection and accurate diagnosis [12]. An elevated count of immature WBCs and a reduction in mature cells may be indicative of leukemia. Techniques such as flow cytometry and chromosomal analysis. These diagnostic procedures are time-intensive and require specialized expertise. However, image processing techniques can assist pathologists in making faster leukemia diagnoses. Currently, many researchers are focused on automating the diagnosis of leukemia, as well as related diseases such as malaria and lymphoma [13].

In light of the growing need for accurate and efficient methods to classify white blood cells and diagnose leukemia, this review aims to provide a comprehensive analysis of recent studies that have employed deep learning and transfer learning techniques in this field. The paper highlights the most commonly used models,

examines their strengths and limitations, and discusses the challenges these approaches face. It also offers insights into future directions that could enhance the performance and reliability of intelligent diagnostic systems in medical applications.

The remainder of this paper is organized as follows: Section 2 provides background information on leukemia, its types, and the importance of white blood cell (WBC) classification in diagnosis. Section 3 presents a detailed review of recent studies applying deep learning and transfer learning techniques to WBC classification. Section 4 discusses and compares the performance, strengths, and limitations of these approaches. Section 5 concludes the paper by summarizing key insights and proposing potential directions for future research in automated leukemia diagnosis.

B. Theoretical Background

The term "leukemia" originates from the Greek words "leukos" meaning white and "haima" meaning blood. It is the utmost frequent type of blood cancer that grows over all the categories of age especially in children. by blood-forming tissues that occur in the bone marrow of humans, where most of the blood is produced[14].

People with leukemia experience rapid growth of abnormal white blood cells, which overcrowd the bone marrow and hinder the proper functioning of normal cells, as illustrated in Fig. 1.

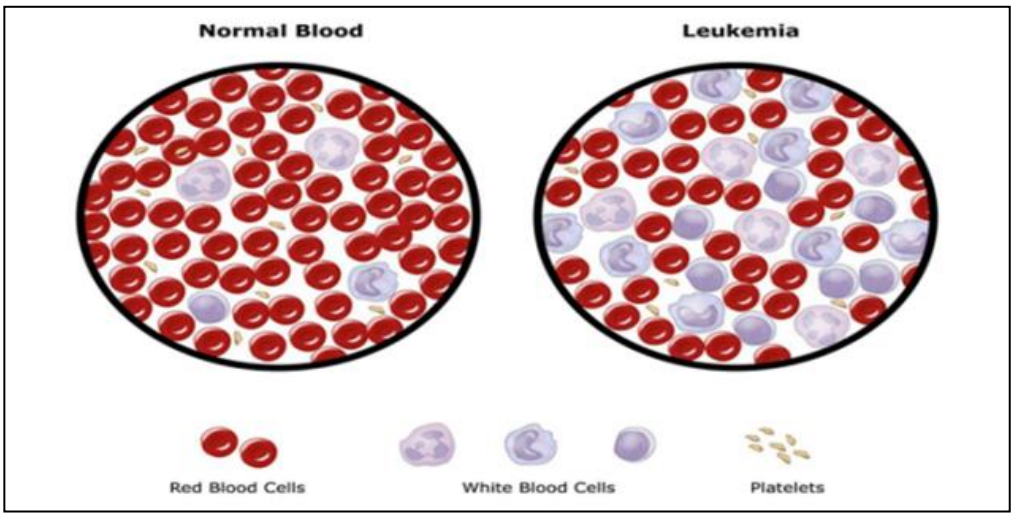

Figure 1. Normal blood vs. leukemia blood

Leukemia is a leukocyte cancer. It is classified as myeloid or lymphoid, Based on the cell lineage, leukemia is classified as either myeloid or lymphoid, and according to how rapidly it progresses, it is identified as either acute or chronic. The four major types include acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL), and chronic lymphocytic leukemia (CLL) [4]. These categories are depicted in Fig. 2.

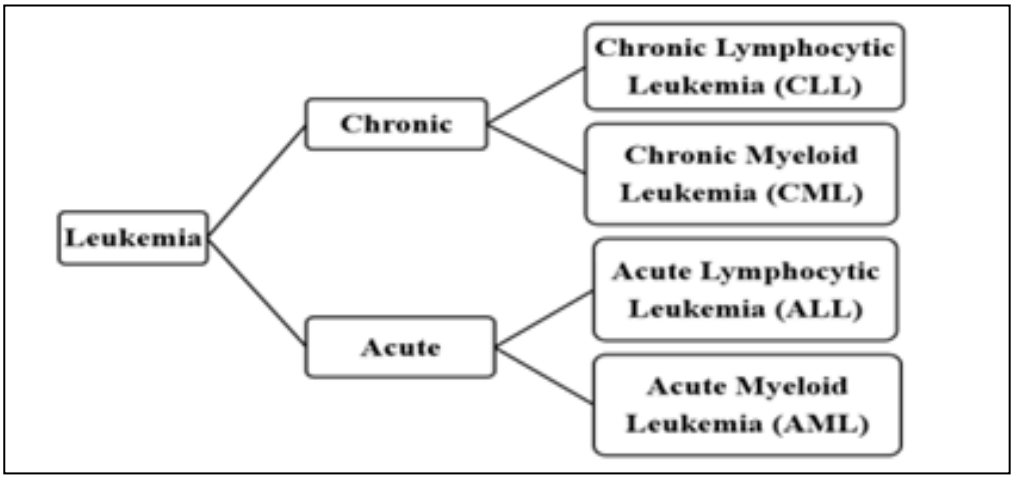

Figure 1. Types of Leukemia

a-Acute Lymphocytic Leukemia (ALL) primarily affects children and is a type of white blood cell cancer caused by the continuous multiplication and overproduction of immature white blood cells in the bone marrow. The symptoms of ALL, which include fatigue, weakness, and joint and bone pain, are similar to those of the flu and other common illnesses, making diagnosis challenging. Acute Lymphoblastic Leukemia (ALL) is classified into L1, L2, and L3 subtypes by the FAB system, based on cell shape under a microscope.[15],[16].

b- Acute Myeloid Leukemia (AML) is a prevalent form of acute leukemia marked by the excessive formation of abnormal white blood cells, and occasionally irregular red blood cells and platelets. Its symptoms vary widely, including bone pain, fatigue, fever, and unexpected bleeding, making it essential to distinguish among its eight identified subtypes for accurate diagnosis [17].

c- Chronic Lymphocytic Leukemia (CLL) is the most frequently diagnosed leukemia among adults in Western countries, with recent progress in treatment driven by novel biological therapies and the identification of molecular markers that help predict disease progression. Risk factors such as working in agriculture, exposure to Agent Orange, and potentially ionizing radiation have been associated with an increased likelihood of developing CLL, though a definitive link to radiation exposure has not yet been established [18].

d- Chronic Myeloid Leukemia (CML) is a hematologic malignancy that mainly affects adults, with only occasional cases reported in children. Diagnosis often begins with a microscopic evaluation of bone marrow samples, while confirmation is usually achieved by examining a peripheral blood smear under a microscope [19].

Recently, deep learning techniques have shown high efficiency in classification tasks across large datasets [20]. Accurate classification of white blood cells is essential for leukemia diagnosis and treatment planning. WBCs are morphologically categorized into lymphocytes, monocytes, neutrophils, and eosinophils (Figure 3), each playing a distinct immunological role [21]. Traditional diagnostic techniques such as flow cytometry and chromosomal analysis are time-consuming and demand expert interpretation.[21].

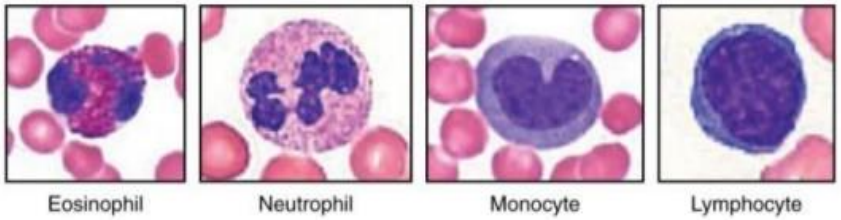

Figure 3. Types of white blood cells

As artificial intelligence and image processing methods have advanced, automated WBC classification has gained traction as a reliable and efficient diagnostic tool. Models for deep learning and machine learning have demonstrated potential to support pathologists by accelerating the diagnostic process and minimizing.

C. Related Work

Recent research on deep learning-based white blood cell classification has shown remarkable results, with models such as VGG16 achieving up to 99.82% accuracy [26], MobileNet reaching 99.36% [26], and ResNet-50 reporting 99.3% accuracy and 99.99% AUC [32]. Hybrid techniques that fuse CNN-based features with handcrafted methods further improved classification performance, surpassing 98% accuracy in some cases [24]. Semi-supervised approaches also demonstrated competitive accuracy (94.4%) using only 500 labeled samples [27]. Vision Transformers (ViT) showed perfect accuracy on high-quality datasets, confirming their robustness in WBC classification tasks [39]. These advancements are summarized in Table 1, which compares deep and transfer learning models across datasets and performance metrics.

Table 1. Summary of Deep Learning and Transfer Learning Models for White Blood Cell Classification

Ref	Aim of the Study	Dataset Info	Technique	Performance Metrics	Results	Conclusion	Strengths	Limitations	Future directions
[22]	Classify WBCs for early leukemia detection	1,200 images, Kaggle, 4 WBC classes	CNN, ANN, KNN, SVM	Accuracy, Precision, Recall	CNN: 93% accuracy	Deep learning significantly improved diagnostic accuracy.	High accuracy, advanced feature extraction	Misclassification of similar types, small dataset	Use transfer learning, diverse datasets, attention-based models
[23]	Classify atypical WBCs in AML	AML Cytomorphology, 18,365 single-cell images	Hybrid: DCAE + CNN	Accuracy, Sensitivity, AUC	Accuracy: 97%, AUC: 99.7%	Superior feature extraction and classification accuracy.	Robustness in feature extraction	Reduced performance for intermediate subtypes	Expand datasets, improve sensitivity

Ref	Aim of the Study	Dataset Info	Technique	Performance Metrics	Results	Conclusion	Strengths	Limitations	Future directions
[24]	Improve WBC classification with hybrid methods	12,507 images, 4 WBC categories	CNN-based (VGG19, ResNet101, MobileNet) + Handcrafted features	Accuracy, Specificity, Sensitivity	VGG19-ResNet101-MobileNet-SVM: 98.40% accuracy	Robust hybrid feature extraction and classification.	Strong overall performance	Challenges with eosinophil and neutrophil classification	Expand datasets, refine feature selection
[25]	Direct leukocyte detection and classification	2,700 detection patches, 3,060 classification images	YOLO v2, CNN	Accuracy, AP	Detection: 96% AP, Classification: 94.3%	Detection: 96% AP, Classification: 94.3%	Avoided preprocessing, effective classification.	High performance, avoided preprocessing	Imbalanced WBC types
[26]	Enhance WBC classification with transfer learning	12,500 images (Kaggle, BCCD	Pre-trained CNNs: VGG16, ResNet50, MobileNet	Accuracy, Recall	VGG16: 99.82% accuracy, MobileNet: 99.36%	Transfer learning addressed data scarcity effectively.	Robust classification across datasets	Computational resource demands	Develop customized architectures for rare subtypes
[27]	Semi-supervised WBC classification	29,721 image patches, 500 labeled samples	Semi-supervised CNN with augmentation	Accuracy	Semi-supervised: 94.4%, Fully-supervised: 97.9%	Reduced annotation workload, robust classification.	Lower dependence on labeled data	Slightly underperformed fully supervised methods	Improve generalization, diverse dataset testing
[28]	Detect/classify WBCs for leukemia diagnosis	1,732 images, 27,184 cells	RetinaNet + ResNet-based ensemble	Accuracy, F1-score, Sensitivity	Classification: 82.93% accuracy, F1-score: 82.02%	Demonstrated strong potential for leukemia diagnosis.	Processed raw images, broad WBC type coverage	Reduced performance for rare cell types	Expand datasets, improve rare cell accuracy
[29]	Improve efficiency and accuracy in leukocyte classification using a CNN-based model.	9,957 training and 2,487 test images across four WBC types.	Customized CNN model without preprocessing or segmentation.	Accuracy, precision, recall, loss.	98% accuracy with low training and testing losses.	Demonstrated potential for real-world healthcare applications with cost reduction.	High accuracy with reduced computational complexity.	Limited to a single dataset.	Expand datasets and refine the model for broader applicability.
[30]	WBC classifica	BCCD, ALL-	VGG16-based CNN	Accuracy	Blast cells:	Effective in differentiati	High accuracy,	Dataset limitatio	Expand datasets,

Ref	Aim of the Study	Dataset Info	Technique	Performance Metrics	Results	Conclusion	Strengths	Limitations	Future directions
	tion and differentiation of leukemia	IDB1, ALL-IDB2 datasets			98.4%, WBC: 96.7%	ng leukemia from leukemoid reactions.	robust performance	ns, improved segmentation needed	enhance segmentation techniques
[31]	Acute lymphoblastic leukemia classification	16,249 images, Kaggle	DDRNet (Deep Residual Dilated Network)	Accuracy, F1-score	Training: 99.86%, Testing: 91.98%, F1: 0.96	Robust classification with advanced feature extraction.	Computational efficiency, robust classification	High-quality data dependence	Expand datasets, refine feature extraction and attention mechanisms
[32]	Improve WBC classification with hybrid models	12,507 images, Kaggle	Pre-trained CNN (AlexNet, ResNet-50, etc.) + SVM	Accuracy, AUC	ResNet-50: Accuracy 99.3%, AUC: 99.99%	Hybrid methods enhanced classification efficiency.	High performance, robust hybrid model	Dataset diversity, computational demands	Enhance generalizability, explore emerging models
[33]	Improving WBC classification	Various studies, datasets unspecified	CNNs, normalized cross-correlation, segmentation, transfer learning	Accuracy	Up to 98.7% accuracy (Acharya et al.)	Emphasized regularization and hybrid optimization for advancements	Variety of techniques tested	Handling duplicate images, multi-class detection challenges, and dataset imbalance	Modified loss functions, hybrid optimizations
[34]	Classifying 4 blood cell types using CNN and transfer learning	Kaggle dataset (9,957 images)	MobileNetV2, VGG16, Xception, ResNet50V2	Accuracy, precision, recall, F1-score, ROC-AUC	MobileNetV2: 98.22% training, 87% testing accuracy	Effective for robust classification	Enhanced accuracy and adaptability	Performance variations for cell types, reliance on pre-trained models	Deploying via mobile applications
[35]	Classifying WBCs into subtypes with transfer learning and	BCCD (12,444 images)	DenseNet201, VGG16, PCA, CNN	Accuracy, precision, recall, F1-score	Fused features: 89.75% accuracy	Improved classification accuracy using feature fusion	Minimized classification errors	Lack of preprocessing, single dataset	Diverse datasets, advanced preprocessing

Ref	Aim of the Study	Dataset Info	Technique	Performance Metrics	Results	Conclusion	Strengths	Limitations	Future directions
	feature fusion								
[36]	Enhancing WBC classification via nucleus segmentation and CNN	BCCD (12,444 images)	HSI, Lab* color transformations, k-means clustering, CNN	Accuracy, precision, recall, F1-score	CNN: 96% test accuracy	Effective against staining variability	Robustness, database independence	Single dataset dependency, no real-world validation	Diverse datasets, broader applications
[37]	Optimizing CNN for leukocyte classification	Augmented BCCD (12,453 images)	Grid Search, Random Search, CNN	Accuracy, sensitivity, specificity	97% validation, 99% training accuracy	High reliability in leukocyte classification	High accuracy, reduced processing time	Dataset dependency	Larger datasets, hybrid models
[38]	Leukocyte classification using transfer learning	Kaggle (12,515 images)	Inceptionv3, MobileNetV3, VGG-19	Accuracy	Inceptionv3: 99.76% accuracy	Outperformed other models	Superior accuracy and robustness	Single dataset dependency	Expanding datasets, broader applications
[39]	Classifying WBC types using Vision Transformers and CNNs	PBC and BCCD datasets	ViT, CNN	Accuracy	ViT: 100% on PBC, 88.36% on BCCD	Demonstrated ViT's adaptability	High accuracy and adaptability	Computational overhead, excluded cell types	Expand classification categories, address data quality
[40]	WBC classification using transfer learning and CNNs	Kaggle dataset (3,000+ images/class)	ResNet50, InceptionV3	Accuracy	>98% (InceptionV3 best)	Strong diagnostic potential	High accuracy, generalization	Single dataset dependency	Hybrid architectures, broader datasets
[41]	Enhancing WBC classification with preprocessing and CNN	IEEE Dataport (3,539 images)	CNN with multi-fold preprocessing	Accuracy, precision, recall, F1-score	CNN: 99.86% accuracy	Preprocessing improved efficiency	High accuracy, efficient training	Small dataset size	Ensemble methods for broader capabilities

D. Discussion and Comparison

The literature review highlights substantial progress in applying deep learning (DL) and transfer learning (TL) techniques for the classification of white blood cells (WBCs), which plays a pivotal role in the early diagnosis of leukemia. Recent advancements in AI-driven diagnostic tools are poised to revolutionize leukemia detection by improving diagnostic speed, accuracy, and cost-effectiveness. Among the most successful approaches, Convolutional Neural Networks (CNNs) , notably architectures such as VGG16, ResNet, and MobileNet, have consistently achieved high accuracy rates, often exceeding 95% across various datasets. Hybrid techniques that combine CNNs with handcrafted features further enhance classification performance, especially when dealing with small or imbalanced datasets [23], [24]. These methods have proven effective in addressing morphological variability and class imbalance. Transfer learning also improves model generalizability across different data sources, as shown in recent work [26]. Moreover, semi-supervised approaches reduce the need for extensive labeled datasets while maintaining competitive accuracy [27]. Vision Transformers (ViT) have also shown impressive results, particularly with high-quality input data, although their implementation remains computationally intensive [39]. Despite these advancements, current models face challenges in classifying rare WBC types and adapting to real-world clinical variability. Therefore, upcoming studies should aim to create more diverse and balanced datasets, design models that are both efficient and interpretable, and incorporate multiple data types to improve clinical usefulness and diagnostic accuracy.

E. Conclusion

This paper provides a comprehensive analysis of recent advancements in deep learning and transfer learning techniques for white blood cell (WBC) classification, Focusing on their use in leukemia diagnosis, the reviewed studies highlight that convolutional neural networks (CNNs), hybrid methods, transfer learning models have significantly enhanced accuracy and efficiency of white blood cell (WBC) classification, often exceeding 95% in terms of accuracy scores. Novel approaches such as semisupervised learning and Vision Transformers sound promising to reduce the reliance on large amount of annotations and to address issues with data imbalance and noise. However, some problems still remain, particularly to develop models for rare types of WBCs or to overcome shortcomings of the available data sets, and ensuring clinical applicability. The above-reviewed literature highlights the use of deep learning techniques for leukemia detection, and it demonstrates that the CNN, the hybrid model, and the transfer learning technique significantly improve the performance of WBC classification both in terms of accuracy and efficiency and report accuracy of over 95%. Recent techniques such as semi-supervised learning and Vision Transformers bring new opportunities, by reducing the amount of annotation, and by handling well imbalanced or noisy datasets. However, challenges still exist, especially in ensuring model generalization to rare WBC types and overcoming constraints posed by limited datasets.

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