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Review

The application of artificial intelligence in the diagnosis and management of anemia

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Abstract

Anemia stands out as the most prevalent blood disorder globally. Various factors can contribute to its development, including insufficient production of red blood cells (RBCs) as well as degradation of RBCs. The functional impairment of RBCs in anemia can result in a wide spectrum of symptoms, ranging from fatigue and weakness to severe, life-threatening conditions. The primary method for detecting anemia is the commonly employed complete blood count (CBC) test. However, for certain cases and to distinguish between different types of anemia, more advanced tests become necessary. Artificial intelligence (AI) has emerged as a technology designed to replicate human intelligence and perform tasks that typically require human cognitive abilities. AI models possess the capability to comprehend patterns and associations, enabling them to recognize and analyze images. In the context of anemia, studies have demonstrated that AI algorithms can analyze images of various physical characteristics such as conjunctiva, palm, tongue, and fingernails. By estimating hemoglobin concentration, these algorithms can predict the presence of anemia. Furthermore, AI systems have also exhibited the ability to analyze clinical data, including laboratory tests and blood smears, to predict anemia and identify specific types. It is worth noting that previous studies in the context if AI applications in anemia have been conducted on relatively small populations. However, the accuracy achieved in these investigations has been satisfactory, suggesting that AI systems could potentially play a significant role in the future of anemia diagnosis and management.

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1. Introduction

The main role of blood circulation is to deliver the blood flow containing all necessary elements such as oxygen and nutrients to cells and take up their wastes (1, 2). The presence of any disorder such as clots, infections, systemic cancers, and alterations in cell numbers like anemia (3-6) could disrupt this system (7). Among all blood disorders, anemia has been shown to be the most common one in human beings (8). Anemia is defined as the presence of any alteration in the function as well as the number of RBCs so they couldn't function properly (9) and deliver oxygen to organs and cells (10). Anemia could be occurred by several triggers. In other words, any reduction in the number of RBCs, the destruction of RBCs, loss of RBCs, loss of hemoglobin, unfunctional hemoglobin, and changes in RBC shape, size, and volume could be a potential factor leading to anemia (11). According to the World

Health Organization (WHO), the prevalence of anemia is 42% and 40% in children under the age of five and pregnant women, respectively (12) which could be due to lack of enough RBC production or the destruction and loss of RBC (13, 14).

The early and precise diagnosis of anemia via affordable and acceptable tools are crucial in order to adopt the most appropriate method to limit the anemia damages (15). The most common method to diagnose anemia is a blood test and the evaluation of hemoglobin concentration, hematocrit value, complete blood count test including RBC count, and RBC parameters (MCV, MCH, and MCHC), and in some cases blood smear (16, 17). Although these methods are the gold standard for anemia detection, they can require, infrastructures, high costs, and labors, be time-consuming, and expose healthcare providers to the hazards of the blood-transmissible diseases (18). Indeed, in several situations, the rapid evaluation of clinical signs of anemia identification such as pulling down the eyelids and assessing conjunctiva pallor could provide quick anticipation of the patient's status; however, due to lack of tools, these methods are not accurate (19, 20). To overcome this challenge, computational systems could be dramatically useful (19).

The initial definition of artificial intelligence (AI) dates back to 1956. Accordingly, AI refers to systems capable of learning and identifying the patterns and relationships which ultimately lead to making decisions for unrecognized data (21). A wide area is covered by AI territory in which machine learning and deep learning are the major subdomains of AI. Actually, the notable capacity of AI algorithms in understanding patterns and recognizing images and faces has drawn several attractions that have broadened its application in sizable aspects of scientific areas such as medicine (22). It has been demonstrated that AI models are able to pave the way for the diagnosis of several diseases including cancers and blood disorders (23). In the context of anemia, they could accurately provide opportunities for analyzing the clinical signs of anemia as well as laboratory parameters; therefore, bring about a way to diagnose anemia in a cheaper and more affordable way with satisfying accuracy (24). The aim of the current study is to discuss how AI systems can facilitate anemia diagnosis.

2. The application of AI systems in the diagnosis and screening of anemia

The detection and screening of anemia allow healthcare providers to identify cases who could be at risk of anemia or classify those with a developed disease. The diagnosis of anemia was traditionally carried out based on laboratory analysis like the complete blood count (CBC) and iron assessment as well as medical history and symptom clinical (25, 26). Providing general information, these tests bring about an initial overview of anemic patients; however, they may not always precisely detect all types of anemia. Actually, this is because some types of anemia could have several varieties in patients, making them difficult to be recognized (18). Recently, the use of computerized algorithms paves the way for several disease diagnoses in the medical context. With this regard, AI systems have been demonstrated to have the capacity in order to detect anemia with higher accuracy, lower costs, and less time consumption (27, 28). Indeed, AI-based approaches to anemia detection have the capacity to improve the efficiency of anemia diagnosis by being trained on large datasets of patient information, including laboratory results, medical history, and clinical data to recognize patterns and associations and make predictions about anemia status (29).

3. Algorithms for anemia diagnosis

Two broad subdomains of machine learning are supervised learning and unsupervised learning which have been utilized in anemia detection. Supervised learning algorithms are trained based on labeled data; however, unsupervised learning ones are trained according to unlabeled data meaning that these systems should recognize patterns or relationships of the data without any pre-existing labels (30). In the context of anemia, several AI algorithms have been utilized regarding anemia diagnosis such as artificial neural networks (ANN), K-nearest neighbor (K-NN), support vector machine (SVM), Bayesian networks, and Decision Tree classifier (31).

3.1. Based on physical characteristics

AI models have shown their potential to analyze metadata of conjunctiva, palm, tongue, and fingernails in order to estimate some anemia-related parameters such as hemoglobin levels (29). With this regard, a Naïve Bayes system that used the waterfall method showed efficacy in the early detection of anemia based on palms and nail images which were converted to YCBCR color (Y is luma [brightness], Cb is blue minus luma [B-Y] and Cr is red minus luma [R-Y]). They demonstrated that the accuracy to detect anemia was 87.5% when various intensities of light were used and 92.3% when the intensity was 5362 Lux (32). Similarly, a study utilized palm images as the data for some machine learning models including K-NN, SVM, Naïve Bayes, Decision Tree, and convolutional neural network (CNN) in order to identify the anemia. After analyzing, Naïve Bayes showed the best performance with 99.96% accuracy and after that, CNN, K-NN, and Decision Tree showed accuracy around 99.9%. Moreover, SVM (a supervised learning model) analysis demonstrated the least accuracy (96.34%) in detecting anemia (33). By evaluating the anterior conjunctival pallor of the eye and the relevant images, a study assessed the capacity of a non-invasive AI system to recognize anemia. It was shown that the computerized cost-effective, easy-to-use, visual system was able to detect anemia with a 78.9% accuracy rate (34). Similarly, a non-invasive AI model was developed to analyze palpebral conjunctiva images of perioperative patients. They demonstrated that the developed deep learning model was able to detect eyelid hemoglobin according to the priori casual knowledge (35).

The ability to detect patients in the emergency department quickly and accurately may improve treatment decisions. In this regard, a deep learning system capable of detecting facial characteristics was trained to detect anemia by analyzing patient videos. They showed that the deep learning model detect first the anemia, second the mild anemia, and third the severe anemia, all of which were based on the levels of hemoglobin. The system could detect anemic status with 82.37% accuracy and 0.84 area under the curve (AUC) while it showed lower efficacy in predicting mild anemia with 68.37% accuracy and 0.69 AUC. In comparison with mild anemia, the performance of the AI system was better in recognizing severe anemia with 74.01% accuracy and 0.82 AUC (36). An interesting study developed an ANN model to estimate the value of hemoglobin by analyzing the color intensity of blood samples (drops) images. The proposed algorithm achieved 95.5% sensitivity and 25% specificity for the detection of anemia in 86 individuals (37). In a study, researchers used AI models in order to assess the status of anemia in individuals by analyzing the sclera and scleral blood vessels extracted from images. By means of SVM, K-NN, Random Forest, and AdaBoost, they demonstrated 73.58% average accuracy for the performance score of the scleral segmentation algorithm. Besides, SVM showed the best performance features from vessels and the entire sclera even with a small number of variants (with a precision of 74.6 and recall of 90.1), implying that AI-based anemia detection is a promising approach with a non-invasive, easy, and quick setup (38). By using several algorithms including CNN, Naïve Bayes, k-NN, SVM, and decision tree the identification of iron-deficiency anemia in children was carried out based on images of palpable palm, eyes conjunctiva, and fingernail. The results were impressive as the best percentages of accuracy and AUC were more than 97% implying how accurate was the AI-based anemia detection. CNN was shown to have the most accuracy and AUC compared with other models and SVM demonstrated the least accuracy and AUC (31). These results further highlight the potential of AI systems in identifying anemia with impressive accuracy and a lower budget compared with conventional methods.

3.2. Based on blood test parameters and clinical data

Some AI systems have been developed to analyze the parameters of blood tests in order to predict the situation of anemia. Accordingly, the presence of some abnormalities in RBCs has been shown to be indicators of anemia. Conventional microscopic methods can detect unhealthy RBCs by analyzing the shape, size, and color of these blood cells; however, there could be some errors and biases. Some developed AI systems are able to identify some other parameters of RBCs like the perimeter, diameter, area, and shape geometric factor by some specific devices. In a study, the accuracy of a SVM classifier to detect several types of RBC including normal, echinocytes, dacrocytes, elliptocytes, spherocytes, stomatocytes, target cells, and unknown cells was determined 93.33%. They imply that the SVM algorithm could facilitate the diagnosis of some types of anemia such as iron-deficiency anemia, hereditary spherocytosis, myelophthisic anemia, and thalassemia (39). Another study developed a three-tier CNN-based model (3-TierDCFNet) in order to evaluate peripheral blood smears of 50 individuals, 50% of which were anemic, for detecting anemia. The deep learning system was able to initially classify patients into healthy and anemic categories and in the following, it could analyze the size, shape, and central pallor size of RBCs in order to indicate the severity of anemia. Accordingly, the accuracy of the proposed AI model in training, validation, and testing was 91.37, 88.85, and 86.06%, respectively (40).

In a study, researchers utilized machine learning models to assess the blood test data in two ways, regression, and classification. In regression, AI systems should estimate the value of hemoglobin based on other blood parameters such as RBC and WBC counts, MCV, MCH, and MCHC amounts. By evaluating three AI algorithms, they showed that Random Forest generated the minimum errors compared with Linear Regression and ANN. In classification, those algorithms should combine all parameters in blood tests including hemoglobin values in order to classify the anemia type. In this regard, Decision Tree showed better performance compared with Random Forest, Naïve Bayes, and ANN. They finally combined Random Forest, Naïve Bayes, and Decision Tree together and revealed that the hybrid machine learning system exhibited better accuracy compared with other algorithms alone (41). Similarly, the application of supervised machine learning models for the prediction of anemia based on blood parameters was investigated. They utilized Random Forest, Naïve Bayes, and Decision Tree (C4.5) algorithms to analyze nearly 15 blood parameters such as RBC count, hemoglobin, HCT, MCV, MCH, and the like. According to analysis, the absolute error of the Decision Tree was higher than the other two algorithms and Naïve Bayes showed more satisfying accuracy in comparison with Decision Tree and Random Forest (96.09% compared with 95.46 and 95.32%, respectively) (42).

By analyzing clinical data and blood parameters such as hemoglobin value and platelet and granulocyte counts, a pre-trained CNN model was able to identify aplastic anemia. The CNN model not only analyzed blood parameters but also evaluated bone marrow images. They showed that the AI system could recognize aplastic anemia with 0.92 accuracy and 0.85 sensitivity (43). In another study, the blood parameters including RBC count, hemoglobin, HCT, MCV, MCH, MCHC, and RDW have been analyzed by AI models with the aim of distinguishing iron-deficiency anemia and β-thalassemia. Accordingly, SVM, K-NN, Logistic Regression, extreme learning machine, and regularized extreme learning machine were utilized to evaluate the blood parameters of 342 patients. Based on the analysis, AI systems showed 95.59% accuracy in distinguishing iron-deficiency anemia and β-thalassemia (44). Similarly, using an ANN model to analyze CBC factors showed that the AI system was able to differentiate iron-deficiency anemia and β-thalassemia 92.5% accuracy as well as 92.33 and 93.13% specificity and sensitivity, respectively (45). These studies indicate the impressive efficacy of AI algorithms in providing a non-invasive and affordable platform to identify anemia and recognized its severity and types which can be used instead of costly and invasive approaches.

Table 1 represented a summary of studies utilizing AI systems in anemia diagnosis.

4. Algorithms for anemia treatments

The precise roles of AI and its direct influences in anemia treatment approaches haven't been illustrated deeply. In other words, the function of AI systems in improving the efficacy of anemia treatments is an untouched area of study for future investigation. Nevertheless, AL systems, machine learning, and deep learning could enhance the outcomes of anemia therapy by providing accurate information regarding the type as well as the severity of anemia. Moreover, these models could be utilized to analyze molecular structures and interactions in order to design effective drugs in the context of anemia treatment (48, 49). Some pathologic conditions such as chronic kidney disease and renal disorders could influence several parts of the body including blood (50). To be precise, a healthy kidney is able to secrete erythropoietin, a stimulator of RBC precursors differentiation. However, in kidney problems like chronic kidney disease, the production of erythropoietin is restricted; thus, the efficacy and frequency of RBCs are reduced, a kind of anemia (51). Understanding the precise status of patients including the inflammation, RBC lifespan, and pharmacokinetics and pharmacodynamics of erythropoiesis-stimulating agents is imperative to limit harmful rise and fall of hemoglobin levels (52, 53). Indeed, machine learning and deep learning models have been utilized to predict responsiveness of patients with renal disorders to iron therapy and erythropoiesis-stimulating agents (54, 55). In patients with chronic kidney disease, a developed machine learning system (ANN) showed notable capacity to predict the value of hemoglobin based on given medical parameters related to hemoglobin in those undergoing secondary anemia (56). Similarly, a reinforcement learning (a subdomain of machine learning) model was used in order to optimize the anemia therapy in hemodialysis patients. The reinforcement learning algorithm analyzed the clinical parameters and medical data and predicted the influences of darbepoetin alfa (a form of erythropoietin) on the concentration of hemoglobin; thus, provided considerable data for anemia treatment optimization (55). The main purpose of utilizing machine learning is to predict the hemoglobin level in

Table 1. Studies using AI systems regarding diagnosis of anemia

AI model (s)	Given dataset	Study population	Efficacy	Best performance	Year	Ref
Based on physical characteristics						
RGB thresholding model	Fingernail	265 patients with hematologic and oncologic disorders	97% sensitivity	RGB thresholding model	2018	(29)
CNN, Naïve Bayes, k-NN, SVM, and decision tree	Palpable palm, eyes conjunctiva, and fingernail	710 anemic and non-anemic patients	More than 98.3% accuracy	CNN	2023	(31)
Naïve Bayes	Palm and nail	NA	92.3% accuracy	Naïve Bayes	2021	(32)
K-NN, SVM, Naïve Bayes, Decision Tree, and CNN	Palm	Children subjects	99.96% accuracy	Naïve Bayes	2023	(33)
RGB thresholding model	Eyes conjunctiva	19 subjects	78.9% accuracy	RGB thresholding model	2017	(34)
Face recognition deep learning	Face characteristics via video	316 anemic and non-anemic patients at emergency depart-ment	82.37% accuracy	Face recognition deep learning	2022	(36)
ANN	Blood drops	86 subjects	95.5% sensitivity	ANN	2023	(37)
SVM, K-NN, Random Forest, and AdaBoost	Sclera and scleral blood vessels	218 anemic and non-anemic patients	73.58% average accuracy	NA	2023	(38)
Based on blood parameters and clinical data						
SVM	RBC characteristics	NA	93.33% accuracy	SVM	2019	(39)
CNN	RBC characteristics	50 anemic and non-anemic patients	86.06% accuracy	CNN	2022	(40)
Random Forest, Decision Tree, Linear Regression, ANN, and Naïve Bayes	CBC parameters	NA	0.02 mean abso-lute error	Decision Tree	2019	(41)
Random Forest, Naïve Bayes, and Decision Tree (C4.5)	CBC parameters	200 test samples	96.09% accuracy	Naïve Bayes	2019	(42)
CNN	CBC parameters and bone marrow smears	547 patients	0.92 accuracy	CNN	2022	(43)
SVM, K-NN, Logistic Re-gression, extreme learning machine, and regularized extreme learning machine	CBC parameters	342 patients with iron-deficien-cy anemia and β-thalassemia	95.59% accuracy	Regular overlearn-ing machine	2020	(44)
ANN	CBC parameters	268 patients	92.5% accuracy	ANN	2019	(45)
Random Forest, Logistic Regression, k-NN, SVM, and linear discriminant analysis	Anemia-related clini-cal data	2013 anemic and non-anemic children	68.53% accuracy	Random Forest	2019	(46)
SVM	RBC characteristics	130 patients	95.92% accuracy	SVM	2020	(47)

order to adjust the dose of erythropoiesis-stimulating agents. A similar study evaluated the ANN model to analyze specific demographic data of patients with end-stage renal disorder in order to adjust the therapy. They showed that the machined learning model was able to increase the value of hemoglobin by 12.6% and reduced the dose of darbepoetin by 27%. Moreover, it could decrease the rate of transfusion, an important action in anemia management (57). **Figure. 1** is depicted to provide an overview of AI roles in the context of anemia.

5. Conclusion and future prospects

Anemia is a common blood disorder that can cause several clinical symptoms including weakness, fatigue, dizziness, and shortness of breath, and it could be life-threatening in some cases. Anemia comprises a vast range of diseases; however, the present method for diagnosing them is based on investigating clinical data, blood parameters, and in some patients, specific medical information such as bone marrow smears. Although these approaches provide a potential opportunity for anemia detection, they could face some challenges such as being time-consuming, invasive, and relatively expensive. AI systems are promising tools paving the way for the detection of a myriad of disorders including blood ones. They could analyze the patterns of large data and learn the associations in order to make decisions; thus, the application of AI models in the context of anemia identification is a non-invasive approach that could reduce the costs of diagnosis with favorable accuracy.

Studies have shown that AI algorithms could be utilized in various ways regarding anemia diagnosis. One of them is the application of AI models as the analyzers of images as they could evaluate the density of blood (such as red color) in images of susceptible areas like conjunctiva, palm, tongue, and fingernails. It was demonstrated that AI models can predict the value of hemoglobin just by analyzing images; thus, they could differentiate individuals with anemia and healthy ones with satisfying accuracy and AUC. Moreover, they have been shown to have the ability to distinguish the severity of anemia. In addition, AI systems have been utilized in studies to analyze blood parameters such as CBC and iron levels, and blood or bone marrow smears in order to learn the patterns and predict the type of anemia. Accordingly, studies showed that AI algorithms can detect iron-deficiency anemia, sickle cell anemia, thalassemia, and aplastic anemia by analyzing clinical data and blood parameters with promising accuracy and AUC.

AI algorithms have shown favorable roles in anemia detection; however, their direct function in anemia treatment requires further investigation.

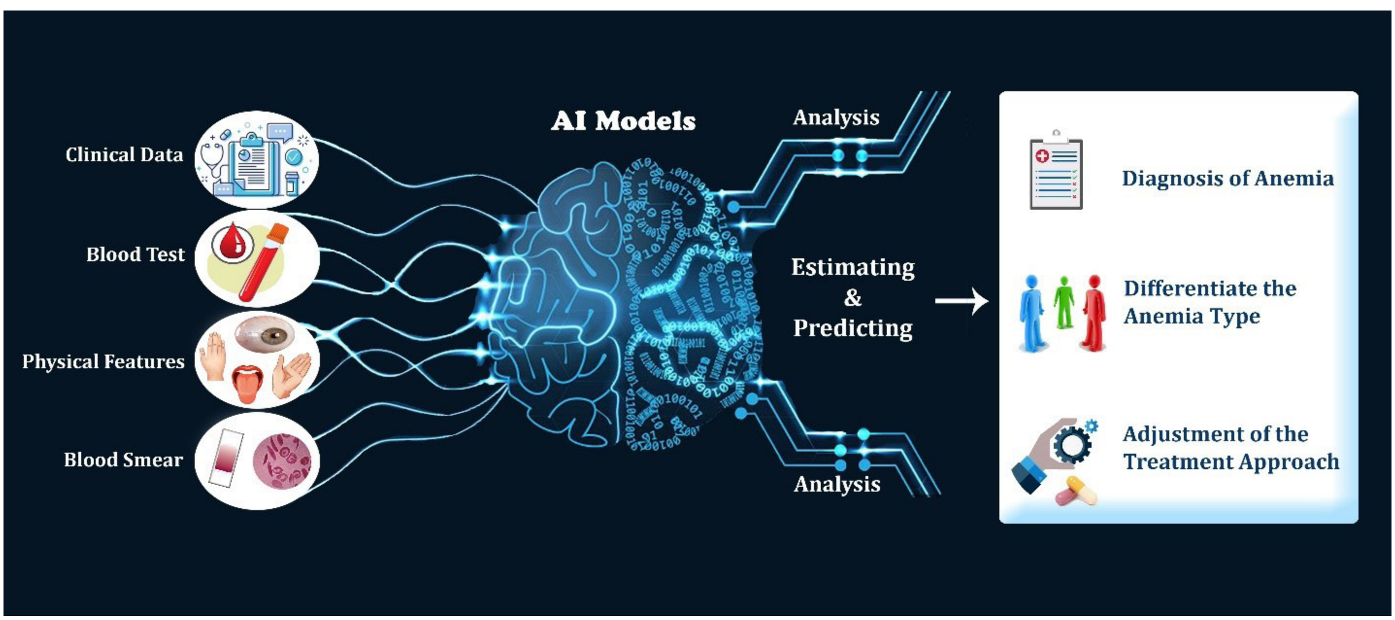

Figure 1. **Schematic illustration of how AI could be used regarding anemia.** Several AI models have been utilized in order to pave the way for anemia diagnosis and treatment. These systems should collect information whether in the testing scale or in the real experiment and learn the patterns and interpret the associations. In the context of anemia, the given data could be the clinical data, blood parameters, physical characteristics such as data from the conjunctiva, palm, tongue, and fingernails, and in some cases, blood smear. AI models could analyze the data and estimate anemia-related factors like hemoglobin values. Consequently, they could predict the diagnosis of anemia, differentiate the anemia type, and in some cases, they could adjust the treatment approach in order to reduce the rate of transfusion and increase the efficacy of therapeutic strategies.

Nevertheless, in some pathologic conditions such as renal diseases, the application of AI systems has shown a potential capacity in predicting the hemoglobin value in order to optimize the dose of erythropoiesis-stimulating agents. Indeed, studies utilized AI models to reduce the rate of transfusion in patients undergoing secondary anemia.

Although using AI models has given researchers and healthcare providers a chance to diagnose anemia in a more convenient and cheaper way, they need to be further investigated in a wider population. It is important to approve the accuracy and efficacy of AI models in a wide range of patients and diverse populations which requires the collaboration of healthcare providers around the world in order to assess AI systems in various clinical settings. Moreover, the establishment of clear and strict guidelines for the implementation of AI tools in anemia diagnosis could address ethical concerns.

Conflicts of interest

The authors declare that they have no conflict of interest.

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