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AI-Powered Noninvasive Anemia Detection: A Review of Image-Based Techniques

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ABSTRACT

Anemia is a serious public health issue affecting over 33% of the world's population. It can result in major health issues such as stunted growth in children, slowed mental and psychomotor development, worse work performance, and increased susceptibility to parasite infections. It is caused by various reasoprismans, including dietary problems, blood disorders, infections and some genetic diseases. Traditional invasive detection methods are expensive, and the results although dependable and accurate but it takes a lot of time, therefore novel, non-invasive methods of detecting and diagnosing anemia are needed. This paper presents a narrative review of research studies interested in the non-invasive detection and diagnosing of anemia and introduces a comparative analysis of how accurate the diagnosing results are. Moreover, it discloses a trend in research regarding a growing awareness in detecting and diagnosing anemia non-invasively by applying different artificial intelligence algorithms on eye conjunctiva, fingernails and hand palm images. Researchers utilized different AI algorithms such as Convolutional Neural Networks, Support Vector Machines, Decision Trees, k-Nearest Neighbor, Naïve Bayes, Logistic regression, random forest, AlexNet, ELM, XGBOOST, LGMBoost, RESNet-50, MobileNet20, EfficientNet-B3, Dense Net 121, CNN Allnet, and ANN. Results of the comparative analysis indicate that the hand palm is the most reliable body region for anemia detection, and the Naïve Bayes is the best algorithm with diagnosing accuracy of 99.96%. This narrative review shows that using non-invasive approach for detecting and diagnosing anemia could provide a possible reliable alternative for quick, affordable anemia screening, especially in non-clinical and low-resource countries.

1. Introduction

Anemia is known to be one of the international public health problems that has consequences on offspring and pregnant women. A study was conducted by the World Health Organization (WHO) implies that 42% of youngsters younger than 6 years old and 40% of pregnant women all over the world suffer from anemia[1]. Iron deficiency, a cause of anemia, influences 33% of the world's total population. Reasons that lead to anemia are some genetic factors, infectious diseases, and iron deficiency [2]. Prompt identification of iron shortage is indispensable for appropriate treatment and inhibition of additional difficulties [3] because it has substantial economic consequences and delays the development of the nation by dropping the labor volume of persons and whole inhabitants [4]. Essential organs including the heart, brain, liver, and kidneys obtain more blood when a person experiences iron deficiency, whereas organs of secondary importance obtain less blood [5]. Iron deficiency takes place when the Hemoglobin (Hb) value in the blood vessels is reduced under the standard threshold of blood in humans, which is frequently mentioned as Red Blood Cell (RBC) deficiency[6]. Anemia is the result of a wide diversity of reasons that can be segregated, but more often coexist. Internationally,the most considerable cause to the commencement of anemia is iron deficiency so that Iron Deficiency Anemia (IDA) and anemia are often used synonymously, and the occurrence of anemia has often been used as a alternate for IDA [7].

The discovery and identification of iron deficiency can be verified through the assessment of the amount of blood Hb or the hematocrit, which determines the number of RBCs to the total blood volume. IDA is believed to be present in individuals with Hb or hematocrit readings of more than two standard deviations below the normal range [8]. It is mostly presumed that 50% of the instances of anemia are due to iron deficiency [9].

Anemia occurs for several reasons such as the level of RBCs within the human body declines, the destruction of the RBCs structure or when the decline of the level of Hb in the RBC to be under the standard threshold, as a result of the increased destruction of one or more RBCs, blood loss, defective cell production or a depleted sum of RBCs. Generally, the level of Hb usually decides whether a person is anemic or not. Advance recognition of anemia is significant to relieve it because if the recognition and handling of anemia are postponed, it permanently destroys different organs in humans, which can cause death in some instance. [10-13]. The extreme drop of the available oxygen delivered to the cells triggers destruction of fundamental organs and then acute anemia must be checked steadily. In critical instances, transfusion of blood is necessary according to the daily reading of the Hb, by extracting a blood sample in a laboratory [14]. According to WHO, anemia is diagnosed when the Hb level is below 13 g/dL in men and when the Hb level is below 12 g/dL in women [15]. Hb level can be measured invasively and non-invasively. Invasive methods are costly, generate medical waste, and require a laboratory environment [11]. Moreover, there are methods that invasively require extraction of blood samples; consequently, they can lead to patients' disconformable, and more likely for infection, or necessitate analysis in laboratories. On the other hand, methods that are non-invasively based are important to individuals who regularly need blood analysis, or prone to blood loss; such methods, in general, detect the paleness of some regions of the body to diagnose patients as anemic or not [16-22]. This paper presents a narrative review of different non-invasive techniques for detecting anemia using eye conjunctive, fingernails and hand palm images and by employing different AI methods.

This paper is organized as follows. The methodology is introduced in section 2. Section 3 describes the results that include many subsections that entail types, causes and symptoms of anemia, AI algorithms utilized in anemia detection as well as body regions of detection are explained, and challenges of non-invasive detection of anemia. Finally, the conclusion and future work of the paper is provided in section 4.

2. Methodology

In this section the methodology of selecting the review papers as well as the inclusion and exclusion criteria is described. Moreover, the databases that are utilized to extract the required papers area stated.

2.1. PRISMA Statement

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) [23] flow diagram is utilized to define the research focus, selected studies, extracted data, and synthesized results. Figure 1 shows different stages of selecting the papers involved in the review reported in the PRISMA flow diagram.

2.1.1. Identification: Research Scope and Key

In this review, Web of Science and Scopus databases [24] are employed to extract the required research papers. The search query that is utilized on Scopus and Web of Science databases is "(TITLE-ABS-KEY (anemia AND detection) AND TITLE-ABS-KEY(conjunctiva OR palm OR fingernails)".

2.1.2. Screening: Search and Selection Process

The initial selection process was conducted using the evaluation of paper titles, abstract, keywords, and publishing year in Scopus and Web of Science databases. In order to add various articles, papers from Google Scholar were included too.

2.1.3. Eligibility: Acceptability Process

The inclusion and exclusion criteria are defined to select articles published in the English language, document type is article and publication date set to selected papers published after 2020. Moreover, other papers are included from Google scholar to have more information about the anemia types and symptoms. The screening process started by extracting the abstract of the articles to ensure compliance with the review subject and excluding other papers that are not. Some papers are extracted too because they are not open access or because the anemia detection body region does not match the regions involved in this review such as using lip mucosa to detect anemia which is outside the scope of the review.

2.1.4. Conclusion: Final Selection

A total of 52 articles have been selected to be included in this review paper. These 52 studies are divided into 14 studies from the Scopus and Web of Science databases about non-invasive detection of anemia, and 38 articles from google scholar. To include other papers about AI models and types of anemia, the 38 google scholar articles are divided into 16 papers about types and causes of anemia, three papers about AI models and 19 about anemia detection.

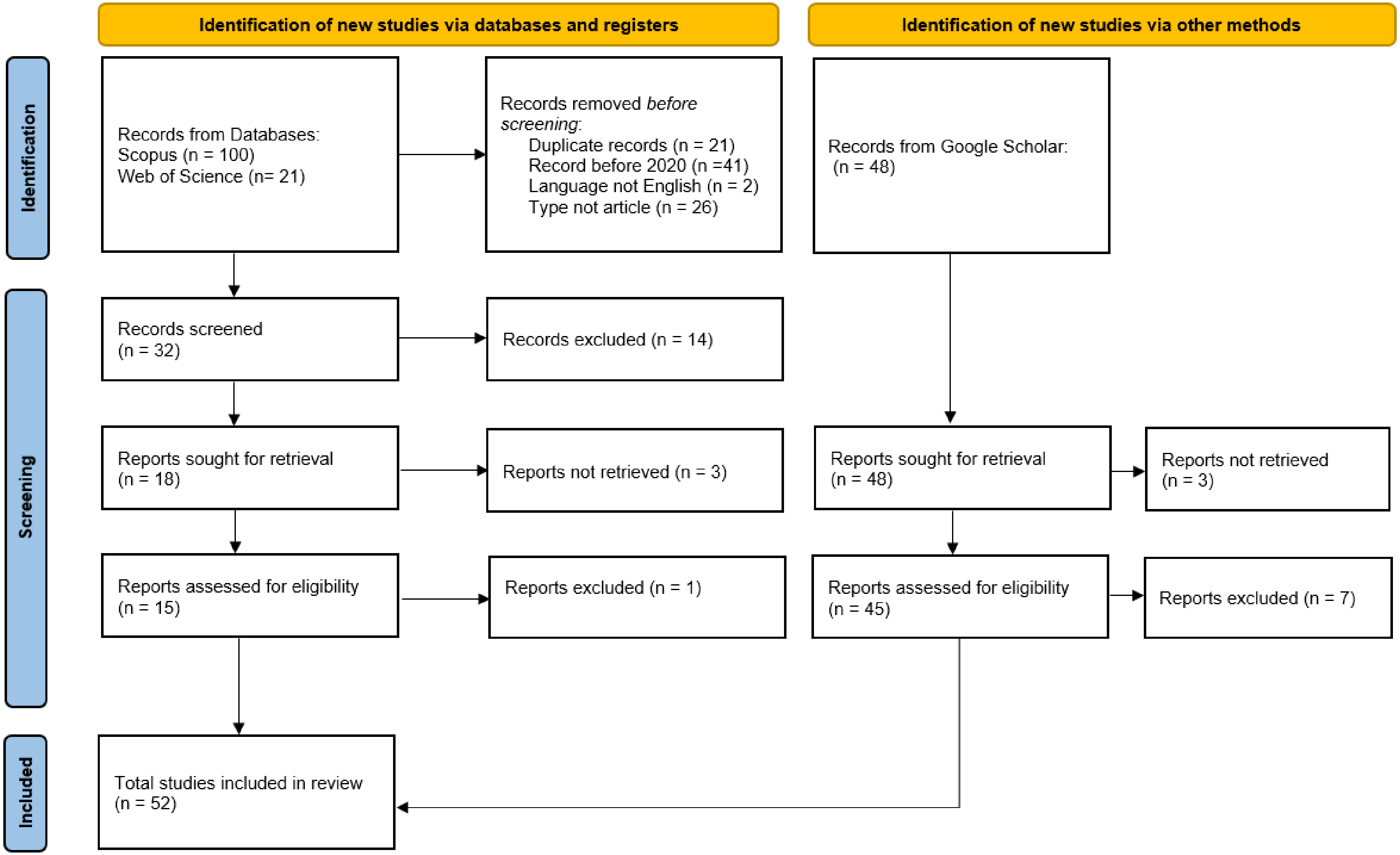


Fig. 1. PRISMA flow diagram.

3. Results

Results are organized as follows, first bibliometric analysis is explored, next is numerical analysis, articles content, a comparative analysis and finally the challenges of detection of anemia non-invasively.

3.1. Bibliometric Analysis

VosViewer [25] is a software application that generates maps according to statistics for the purpose of visualization and exploration. It is used to visualize the important keywords within the selected research papers and find the relation between them as shown Figure 2.

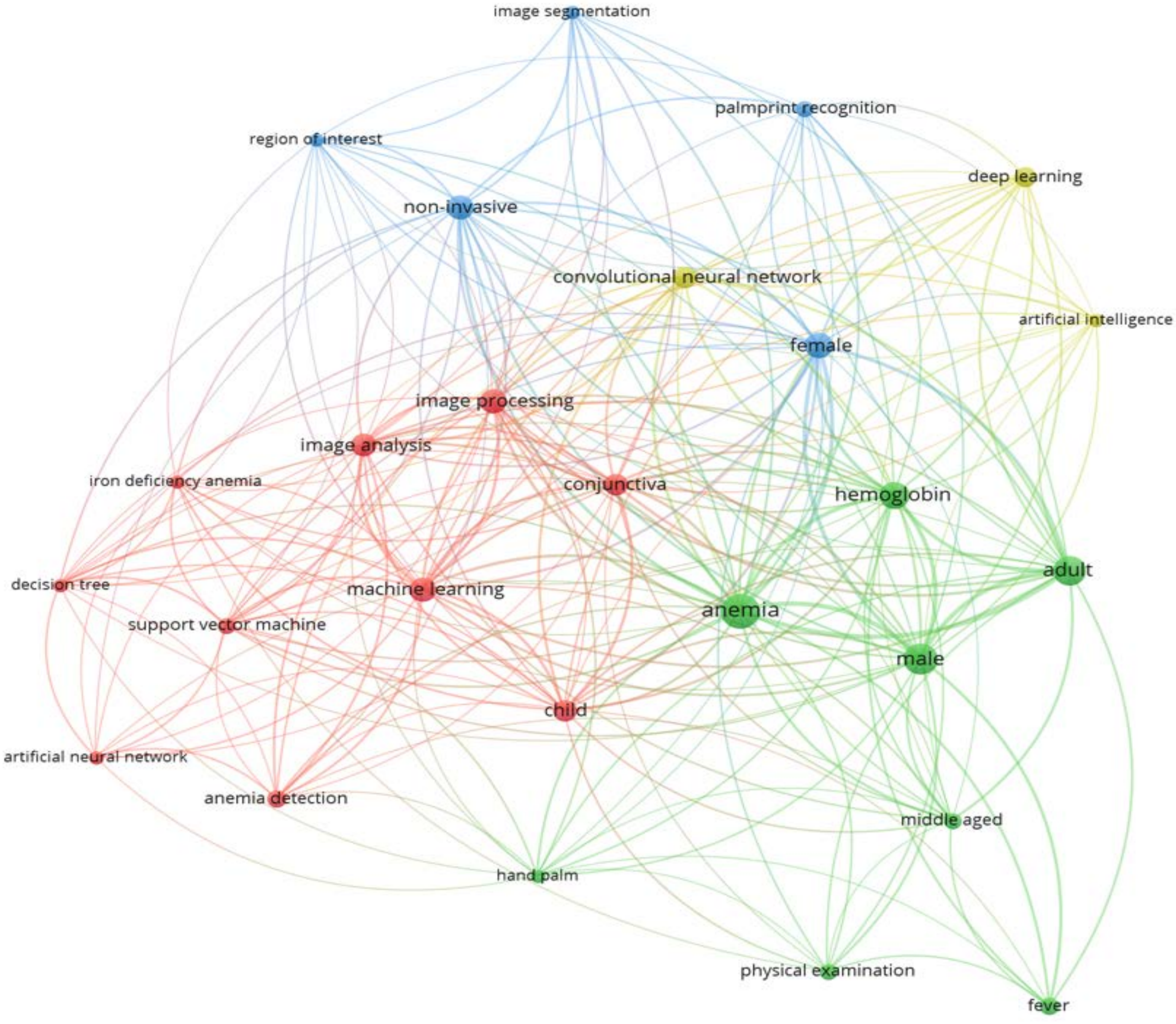


Fig. 2. VosViewer: Relation between keywords

This visualization represents the connections between keywords and their occurrence rate within the selected papers that are contained in the review. Each connected color represents a cluster of keywords. Each node represents a keyword, or a term used within the paper and the lines connecting them represent the relation between them and how often they appear in the same context. The size of the node indicates the importance of the word. The bigger the node is, the more frequently it was used [25]. Four clusters are observed with the node named "anemia" has the biggest size in the green cluster which means it has been mentioned frequently throughout the papers. Moreover, machine learning, image analysis and image processing nodes are big in the red cluster. Furthermore, non-invasive node is the biggest within the blue cluster which is an indication that the selected papers thoroughly comply with the aim of the presented review. Furthermore, Figure 3. shows relationships between authors of different papers.

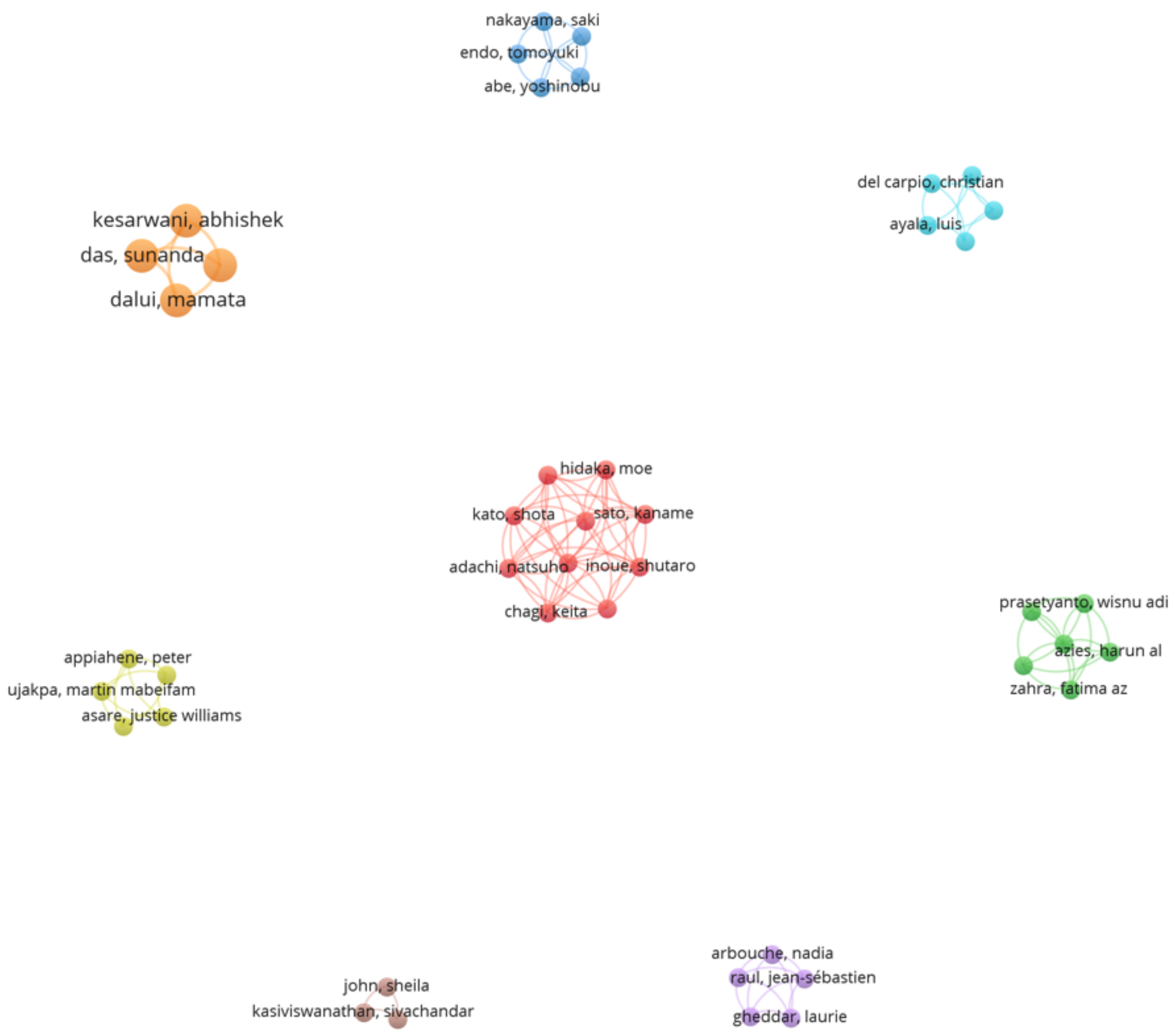


Fig.3. VosViewer: Relation between authors

The visualization shows that there are eight clusters represented by different colors. The orange color cluster has the biggest nodes size, which reflects the highest contribution of its researchers in publishing papers related to anemia and non-invasive detection using different AI methodologies. Moreover, no inter-relations between different clusters are observed which indicates no international cooperation exists in this kind of research.

3.2. Numerical results

In this subsection, numerical analysis of extracted data from the selected papers is presented. Figure 4 shows the distribution of publishing papers over the years starting 2020 until 2024.

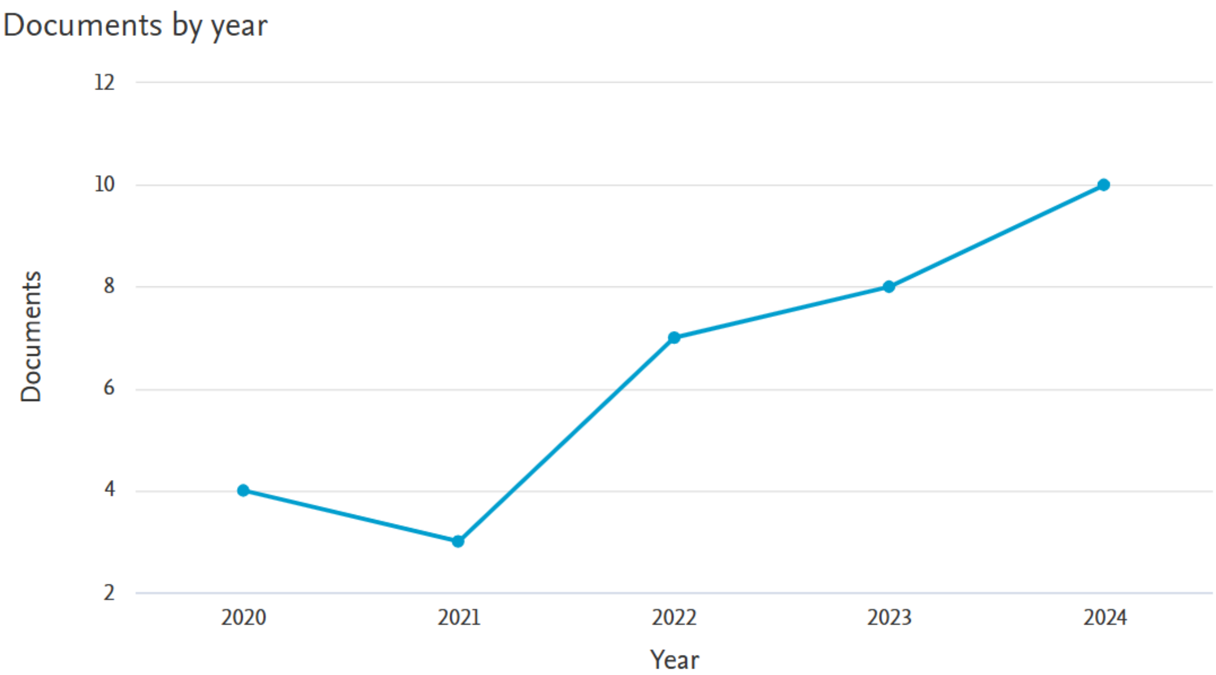


Fig. 4. Papers distribution per year.

Although the published papers show a decline in 2021, there is an overall increasing trend depicted in Figure 4. The decline in publication is expected to be because of COVID-19. The overall trend shows a growing curiosity in this area of research. Moreover, the top fifteen productive countries in publishing papers about non-invasive anemia detection are depicted in Figure 5.

It shows a geographic representation of scientists' interest in finding different non-invasive approaches for anemia detection. India is ranked the first with 12 published papers, followed by Ghana with six papers and Japan with four papers. It shows also that the used patient datasets were mostly from India and Ghana. Moreover, Figure 6 shows a pie chart for the distribution of articles by subject area.

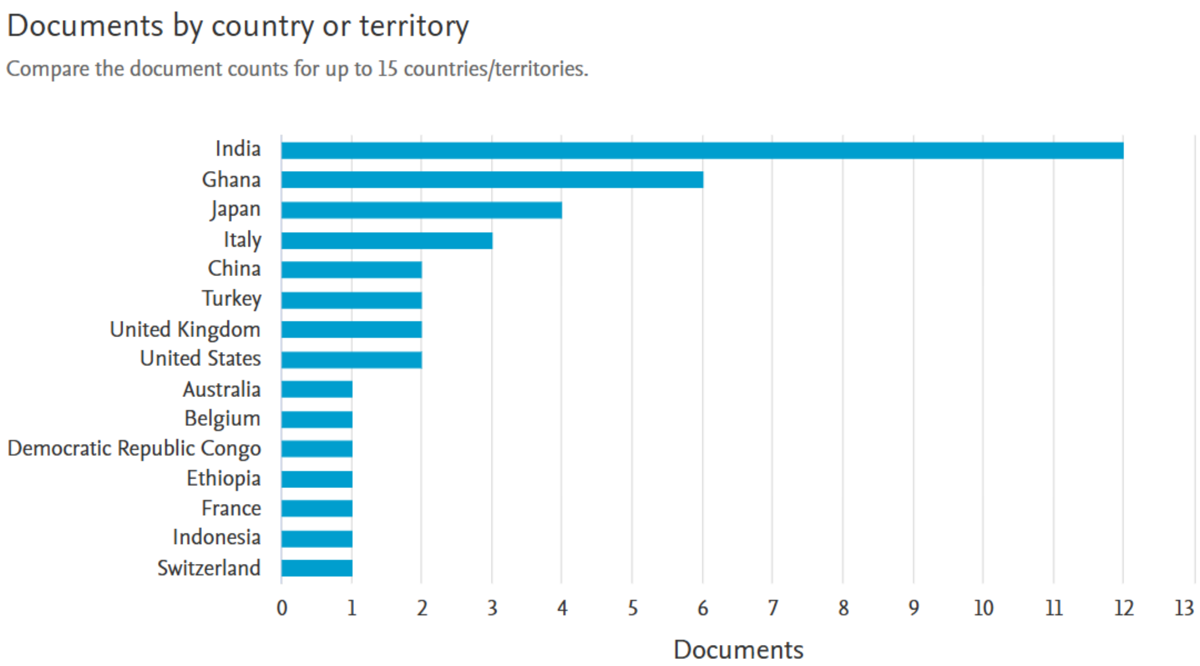


Fig. 5. Top productive countries [24]

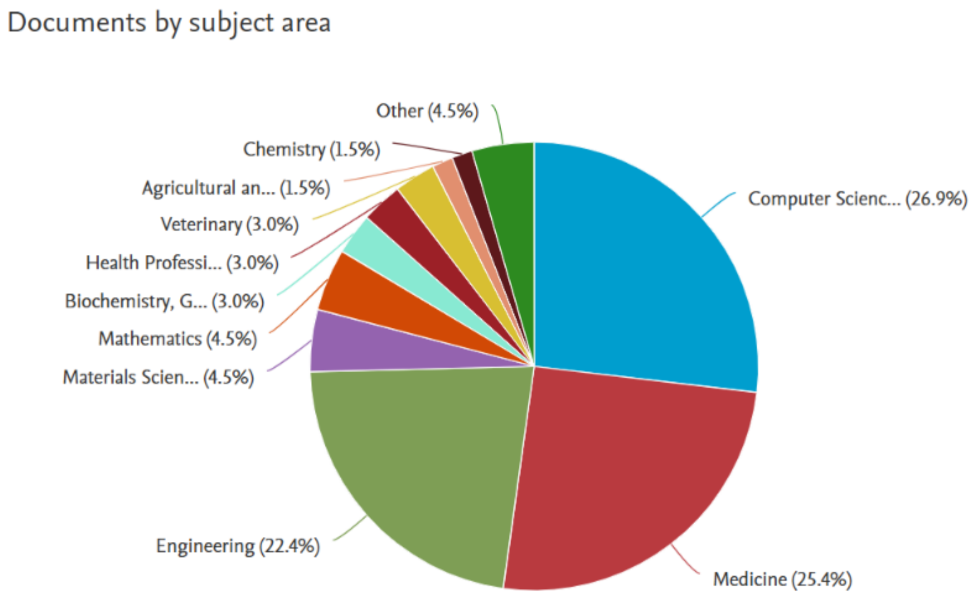


Fig 6. Subjects pie chart [24]

The pie chart shows the fields included in the studies, mostly computer science and engineering with 26.9% and 22.4% respectively, as the novel, non-invasive method focuses on utilizing different AI models to detect the anemia non-invasively. The medicine field comes in the second rank with 25.4% as anemia is a disease that needs medical knowledge to accurately be detected. There are also some other fields like chemistry, mathematics, materials science and biochemistry that are also involved in the research.

3.3. Articles contents

3.3.1. Anemia: Definition, Types, Causes & Symptoms

Anemia has various types, as shown in Figure 7. Its occurrence is due to the various

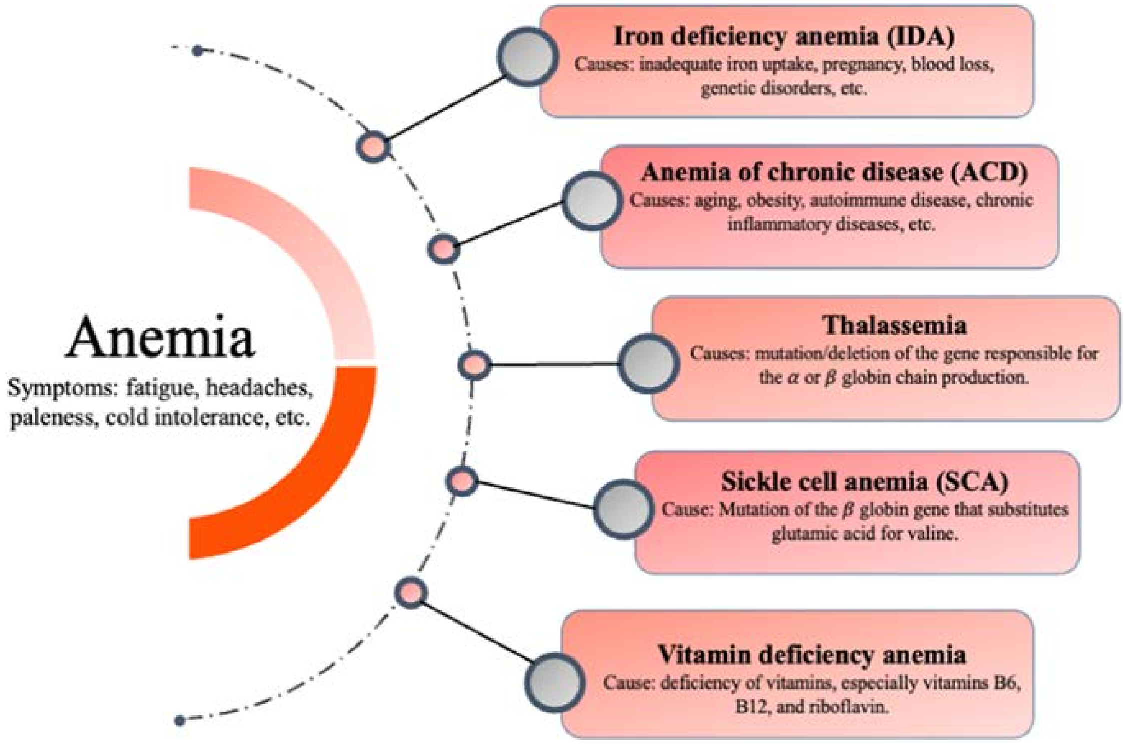


Fig 7. Anemia Types [27]

RBC shortcomings such as defects in production (aplastic anemia), maturation (megaloblastic anemia), Hb synthesis IDA, genetic of Hb maturation (thalassemia) or due to the synthesis of abnormal Hb (haemoglobinopathies, sickle cell anemia and thalassemia) and physical loss of RBCs (hemolytic anemias) [26,27].

3.3.1.1. Iron-Deficiency Anemia (IDA)

IDA is the utmost type of anemia and the most common nutritional lack worldwide [28], it is a medical condition where the iron levels are very low. Adolescents and women before menopause are more likely to suffer from this type of anemia. Pregnancy or childhood growth spurts are the main causes of anemia due to iron shortage, heavy menstrual cycles, inadequate iron absorption, gastrointestinal bleeding, dietary variables (iron deficiency or a limited diet)

[10,27], it can also occurred as a result of medication of various medicines such as Non-Steroidal Anti- Inflammatory Drugs (NSAIDs), which are known to be frequent drugs utilized for reveal pain, fever, and other inflammatory ailments [27].

Its symptoms are tiredness, lethargy, feeling faint and becoming breathless easily, headaches, irregular heartbeats (palpitations), altered taste, sore mouth and ringing in the ears [10]. IDA is of wide drawbacks on the immunity system, for example, impaired B-cell and T-cell work, and lowered the phagocytosis and macrophage-killing capability. Moreover, it can lead to an increment of danger of infection and malaria [27].

3.3.1.2. Anemia Of Chronic Disease (ACD)

ACD is another type of a widespread type of anemia globally, following IDA. ACD is frequently associated with chronic inflammation, autoimmune diseases, cancer, and kidney failure [29]. It arises as a result of the failure of the bone marrow to manufacture enough RBCs despite the existence of sufficient reticuloendothelial iron [27]. The incidence of ACD is increasing, particularly due to an aging population and the rising prevalence of chronic diseases. It can affect up to 40% of patients with solid tumors and nearly 100% of those with leukemia or lymphoma

Its Symptoms are fatigue and weakness, pale skin, shortness of breath, dizziness or lightheadedness, heart palpitations and in some cases cognitive Impairment. While these are the main ACD symptoms, there are also common anemia, so a thorough diagnostic process is essential to differentiate ACD from other anemia types [29], there are other factors such as the level of serum iron and transferring saturation considered as significant for differentiating ACD from further anemias [27]

3.3.1.3. Thalassemia

A genetic blood illness called thalassemia results in the body producing fewer healthy RBCs and less Hb. Alpha- and beta-thalassemia are the two main forms of thalassemia [30]. The most severe type of beta thalassemia is known as Cooley's anemia, while the most severe form of alpha thalassemia is known as alpha thalassemia major or hydrops fetalis. Thalassemia is one of the most common genetic disorders worldwide and is particularly prevalent in regions such as southern China, Southeast Asia, India, the Middle East, Africa, and the Mediterranean. Each region has its own unique spectrum of thalassemia mutations [31]. Hb in RBCs is of two types of chains of protein called: alpha and beta globin. In case someone’s body is not capable of producing sufficient quantities of these chains, the formation of RBCs dramatically influences and consequently, they won’t keep sufficient oxygen. On the other hand, the process of making Hb protein chains in the body is controlled by genes. If such genes are missing or changed, thalassemia occurs. Thalassemia can be transferred to children from their parents through genes [30, 31].

3.3.1.4. Sickle Cell Anemia

Sickle Cell anemia is an autosomal recessive disorder caused by a mutation in the β-globin gene of the Hb. In this mutation, the substitution of glutamic acid by valine occurs, resulting in the production of Sickle Hb (HbS) molecules, which interact with adjacent HbS molecules under deoxygenation conditions and create HbS polymers [27]. Sickle is inherited in an autosomal recessive pattern, meaning that a person must receive two copies of the sickle cell gene (one from each parent) to develop the disease. Individuals with one sickle cell gene and one normal gene are carriers (sickle cell trait) but typically do not show symptoms [32]. It can lead to serious complications, including stroke, acute chest syndrome, organ damage, and increased risk of infections. Sickle cells have a shorter lifespan than normal RBCs, leading to chronic anemia [33].

Sickle-shaped cells can block blood flow in small blood vessels, leading to painful episodes known as "sickle cell crises." Other symptoms may include anemia, fatigue, swelling in the hands and feet, frequent infections, and delayed growth in children [32,33].

3.3.1.5. Vitamin Deficiency Anemia

Vitamin deficiency, also known as nutritional anemia, is deemed to be one of the most communal nutritional illnesses globally, mostly widespread in the low-income countries [27]. For the purpose of ensuring the standard construction of blood cells, some vitamins like riboflavin (vitamin B2), folic acid, vitamin A, vitamin B6, and vitamin B12 are essential, where the role of vitamin C and E work as antioxidants by lessening the free radical’s existence. Deficiency of Vitamin B12 leads to Pernicious anemia [34], this vitamin is found in milk, fish, meat and eggs. This type of anemia commonly arises in senior individuals. Women are prone to this type of anemia than men, and it inclines to occur in families [34].

Its Symptoms differs based on the vitamin that is lacking but some common vitamin deficiency anemia symptoms are psychological problems like depression, confusion, difficulty with memory or even dementia and Nervous problems like numbness, pins and needles, vision changes and unsteadiness.

3.3.2. AI Algorithms & Anemia Detection Regions

3.3.2.1. AI Algorithms

In this subsection, different Artificial Intelligence (AI) algorithms that have been utilized throughout the selected papers in this review for the purpose of non-invasive anemia detection are elaborated as shown in Figure 8.

- *Convolutional Neural Networks (CNN)*

CNN, shown in Figure 9., is a type of Deep Learning neural network architecture commonly used in Computer Vision. Neural Networks are used on various datasets like images, audio, and text. It is composed of a dual of main blocks: first block is “feature extraction”, that are contains diverse and important data which influence in the increment of data accuracy and precision and targets the intends to abstract vibrant features from the data, and the second block is “the classification layer”, which takes place after the abstraction of significant features in data through the utilization of neurons that are fully connected. [11]. In the step of extracting the significant features there are diverse descriptions that are being used in order to accuracy enhancement of the processed data. Next to characteristics extraction, it searches for critical information extraction. CNN can be mathematically modeled as presented in equation 1:

$$z = w^T . x . b \tag{1}$$

Where x is the input, w is the weight, and b is the bias. The share is selected randomly to activate the matrix equals to w. In contrast, the rule that is known as "back-propagation" can be mathematically modeled as in equations 2 [6]:

$$f'^{(x)} = sigmoid(x)[1 - sigmoid(x)] \tag{2}$$

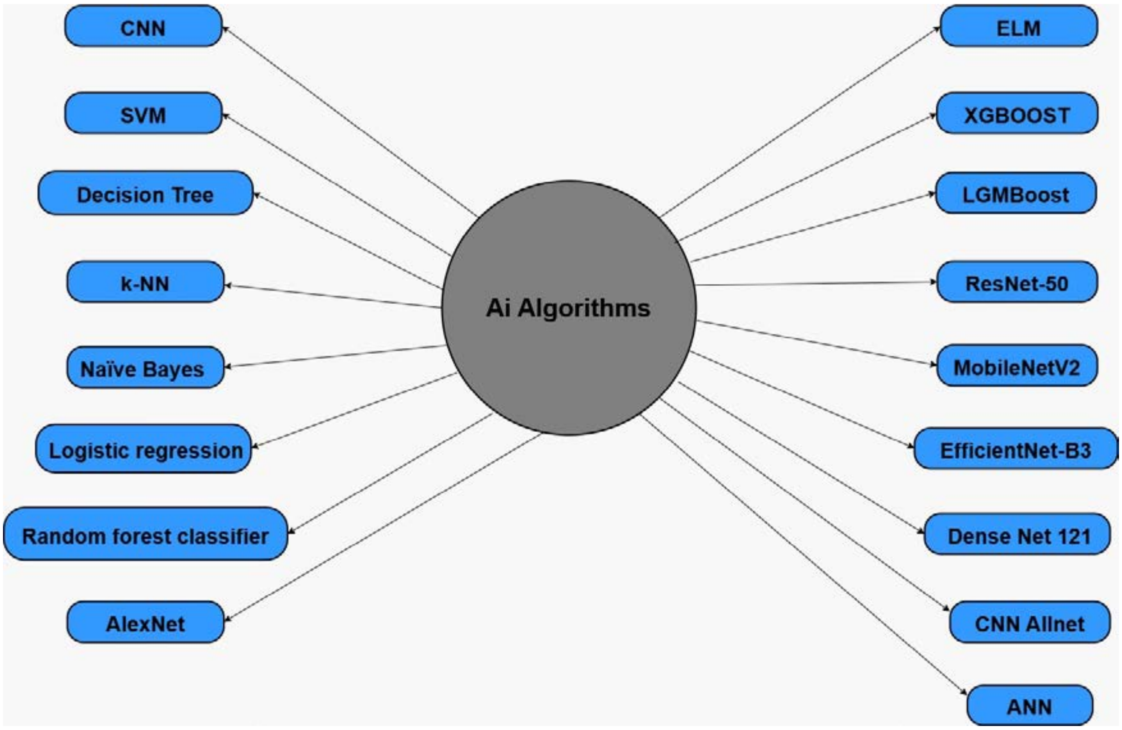


Fig. 8. AI models utilized in non-invasive anemia detection.

Images' features are recognized by many filters to enable objects classification. CNN contains a kernel edge that highlights pixels by utilizing differential output of big pixels, because these extracted features with the CNN scheme are accountable for the kernel. [12]

- *Support Vector Machine (SVM)*

SVM, shown in Figure 10., is a powerful machine learning algorithm widely used for both linear and nonlinear classification, as well as regression and outlier detection tasks. It is particularly effective because they focus on finding the maximum separating hyperplane between the different classes in the target feature, making them robust for both binary and multiclass classification. SVM has separability of data assumption that means it can be divided into many groups using some types of separator functions. [11]. It uses the statistical learning theorem and deeply expands the "separability" principle according to several bases.

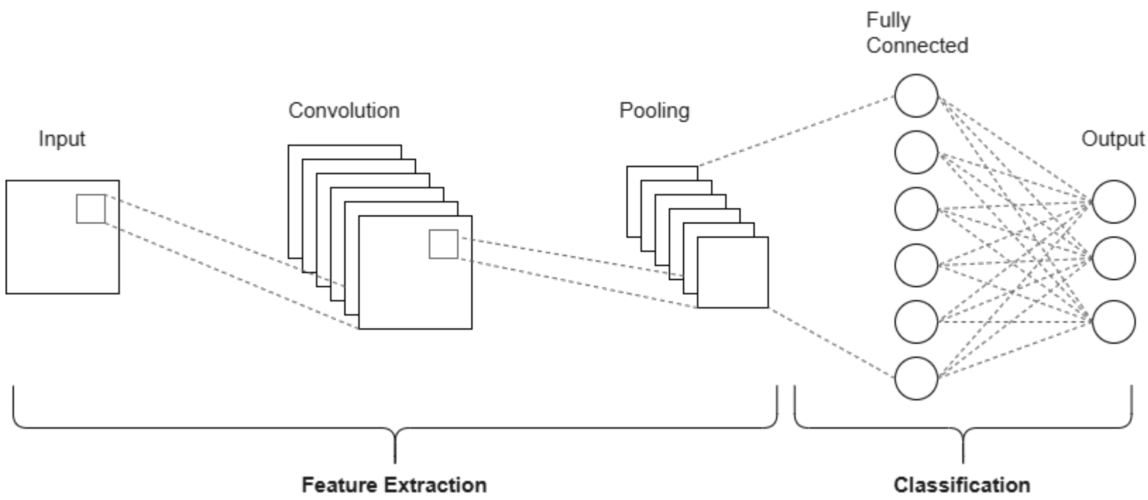


Fig 9. The architecture of the Convolutional Neural Network

SVM has a hyperplane that is denoted by a vector weight (w) and a bias (b) that can be mathematically modeled as in equations 3,4 and 5 [36, 37]:

$$w \cdot x + b = 0 \quad (3)$$

$$w \cdot x + b = -1 \quad (4)$$

$$w \cdot x + b = 0 \quad (5)$$

After the emission of the hyperplane function, it is used in model training, validation and testing. It can be mathematically modeled as in equation 6 [38]:

$$f(x) = sign\,(w \cdot x + b) \quad (6)$$

In case of using the kernel function, equation 6 can be mathematically introduced as in equation 7 [39]:

$$f(x) = sign\,(\sum_{i=1}^{N} a_i y_i k(x_i, x) + b) \quad (7)$$

Usually, the utilized settings are as follows: value of $cost\ (c)$ is 100, the 100 iterations for the sigmoid, 1.10 for epsilon of regression (ε) and 0.1000 for the numerical tolerance. [12]

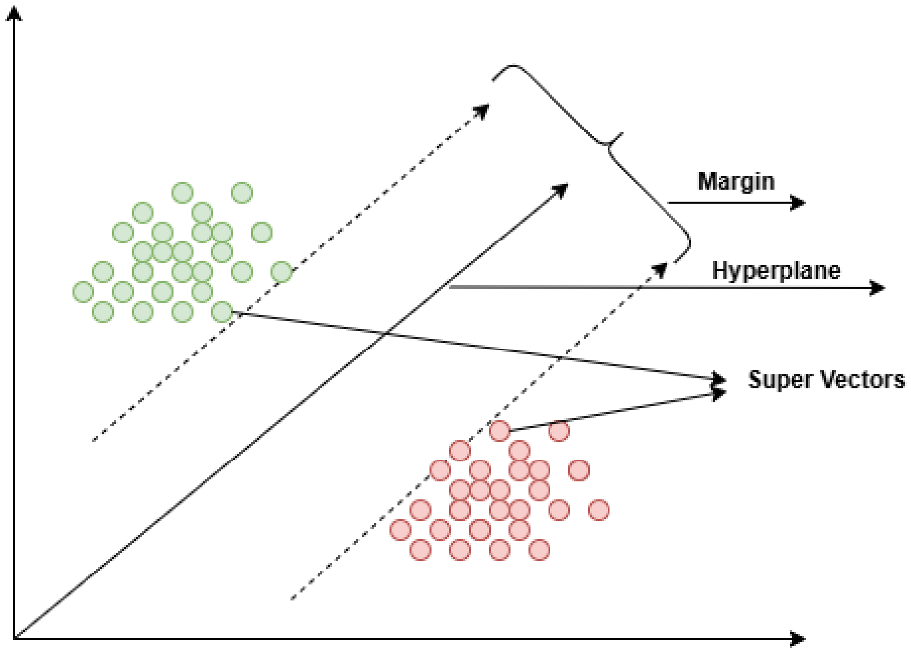


Fig 10. The architectural structure for the SVM

- *Decision Tree*

Decision Tree is a widespread and prevailing method utilized in numerous areas like statistics and machine learning. They afford a strong means of decision making according to the data identifying variables relationships. Each branch of the tree, as shown in Figure 11, indicates attributes values, as it represents tree nodes. Usually, the settings are as follows: the number of trees are at least 100 [11]. Classification is used whenever the order of the tree is from the root nodes to the leaf nodes. The Decision Tree is mathematically expressed as shown in equation 8 [6,39,40]:

$$H(s) = [-P \, log\, 2\, (P+) - [-P \, log\, 2\, (P-)] \quad (8)$$

The gain of the information can be denoted as in equation 9:

$$Gain(S, A) = H(s) \sum_{|s|}^{|Sv|} H(Sv) \quad (9)$$

Its effectiveness for diverse variable analysis despite simplicity is notable. The identification of divided data into segments like branches is accomplished by different tools according to the utilized method of operation. Attributes values are represented by tree branches, instead, tree nodes represent the attributes. [12]

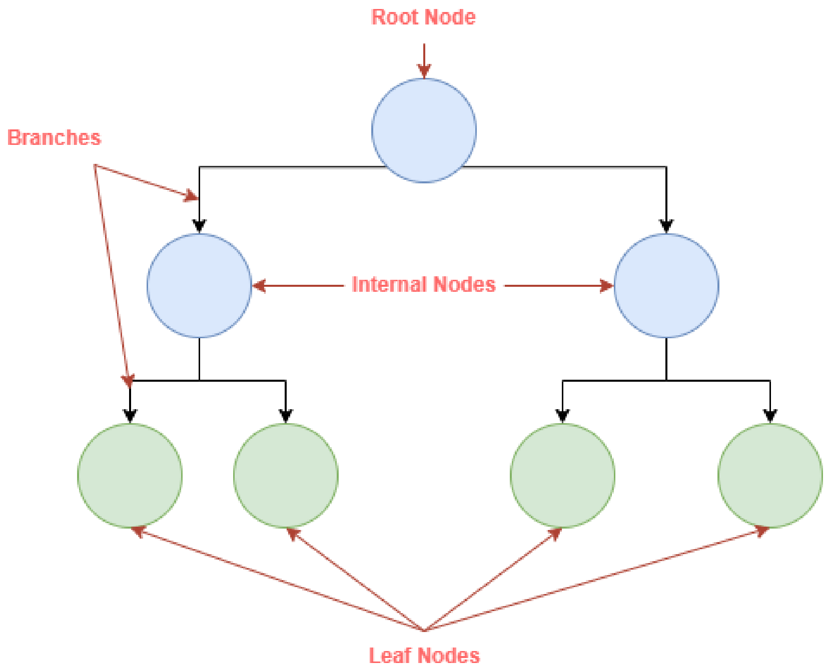


Fig 11. Decision Tree architectural diagram

- *The k-Nearest-Neighbor(k-NN)*

k-NN is a machine learning method of type "supervised". It is employed to tackle classification and regression problems. The "k" in k-NN represents a small positive integer. The decision is being made based on the neighbors. k=2 is a common value to locate the neighbors that are closest in the class. The distance between the feature vectors and their nearest neighbors is being computed and produce artificial data points not the same as the real data points. [11]. It can be mathematically modeled as in equations 10 and 11 [6, 30,41,42]:

$$d(x,x') = \sqrt{(x, -x_1)^2 + div + (x_n + x_n')^2} \tag{10}$$

$$P(y = j \mid x = x) = \frac{1}{k}\sum_{i \in A} I(y^i = j) \tag{11}$$

- *The Naïve Bayes Algorithm*

Naïve Bayes classifier, as shown in Figure 12, is a family of algorithms based on Bayes' Theorem. Despite the "naive" assumption of feature independence, these classifiers are widely utilized for their simplicity and efficiency in machine learning. It has the assumption that no relationship exists between the existence and lack of an attribute, and it can work with small training dataset to be used for variables values mean and variance calculations, meanwhile fields are being split into bins that are distinct and objective value fields. [11]. The Naïve Bayes can be mathematically modeled as in equation 12 as [6,39]:

$$p(c\ /\ x) = P(x\ /\ c)P(c)/P(x) \tag{12}$$

It is known as a probabilistic classifier as it shows great impartiality expectations founded on probability models. Nave Bayes can effectively be generalized because it has no hyperparameter for adjustments.[12]

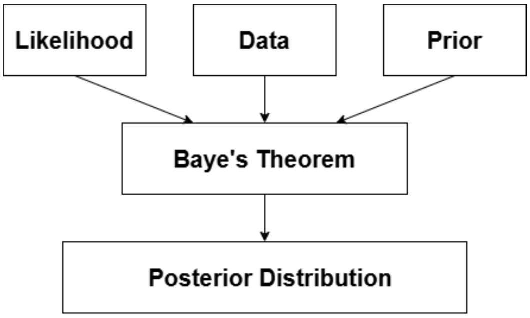


Fig 12. The Naïve Bayes flowchart

- *Artificial Neural Network (ANN)*

ANN takes the human brain structure, and the training dataset helps it in gaining knowledge. It contains three different layers that are the output, the input and the hidden layer. The role of the first layer is to obtain the input, the second layer role is to make the calculation, and the last layer role is the final output prediction. Different channels connect the neurons in various layers. These channels are known as "weight" that are assigned number for each node.

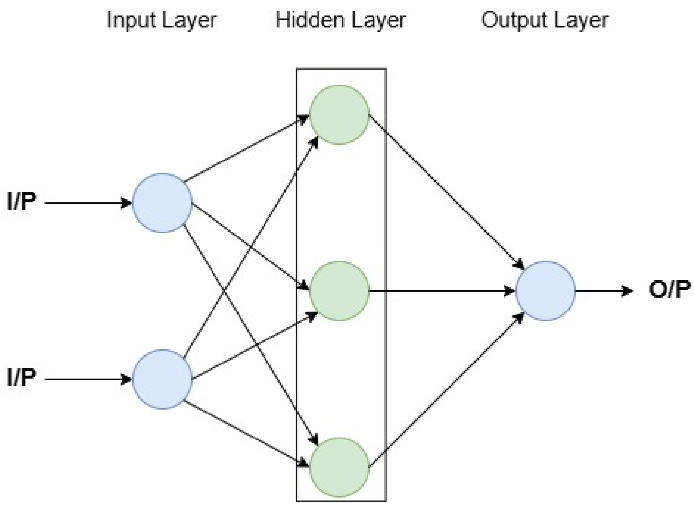


Fig 13. ANN Architecture

Such wights are multiplied by the corresponding input values then the summation is fed to the second layer as depicted in Figure 13 [19]

Another value called "bias" is being added to the summation. Where it is transferred through an activation function and based on its output, the activated neuron is determined. This is called forward propagation. The role of the activation function is the transformation of signal inputs of every node into outputs. The most probable neuron decides the output. The network's actual and predicted outputs are compared to each other's. Back-propagation is utilized for sending system messages for neurons weights change in case the outputs are dissimilar. Achieving the required accuracy is the main aim of the method [19].

- *AlexNet*

AlexNet is a CNN architecture. In Figure 14, there are 3 fully connected layers, 5 conventional all form 8 layers. The learning process of AlexNet consists of 60 million parameters, such parameters affect overfitting.

There are several methods to avoid overfitting that are utilized by AlexNet such as the ReLU activation function, dropout layers and data augmentation. Feature map's number, the filter size, pooling layers' types, activation function, neurons and dropout rate are the hyper parameters of AlexNet.[39].

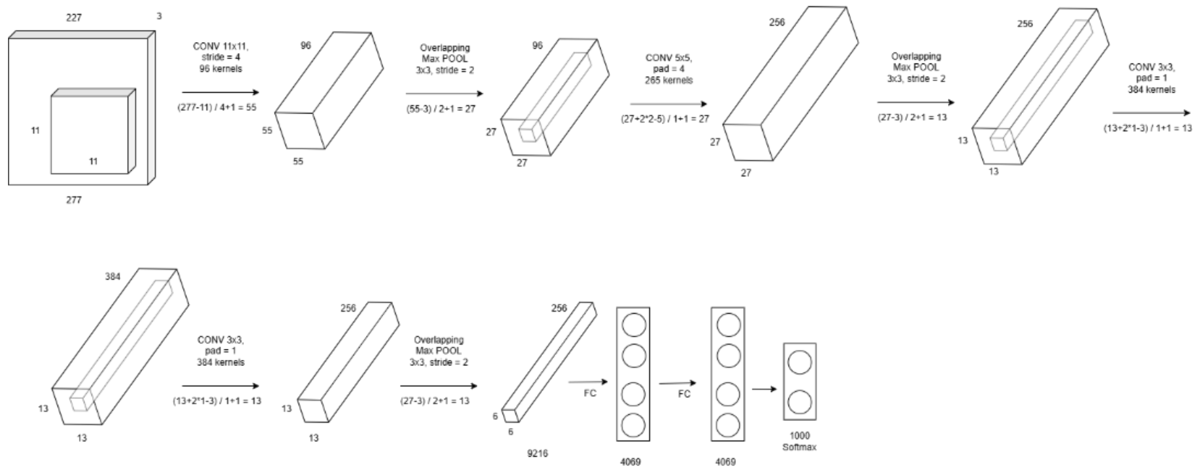


Fig 14. AlexNet Architecture

- *Logistic Regression*

Logistic Regression (LR) is used for binary classification as a statistical method. It creates a model that is based on the relationship between different variables that are binary outcome and predictor variables. Balanced datasets are used for the implementation. The outcome probability is estimated using the logistic function. LR can be mathematically modeled as in equation 13:[44]

$$P(y=1) = \frac{1}{\left(1+e^{\wedge}(-z)\right)} \qquad (13)$$

- *Random Forest*

The Random Forest (RF) is based on building many trees to train the model on the dataset. Every one of the trees is being trained randomly using the training data. In order to avoid overfitting, bagging is utilized. Two methods are used for prediction generation one of these methods is output averaging and the other is classification voting to improve robustness and precision. RF can be mathematically modeled as in equation 14: [44]

$$\hat{Y} = model(F1(x) + F2(x) + \cdots + Fn(x)) \qquad (14)$$

- *Extreme Learning Machine (ELM)*

The Extreme Learning Machine (ELM) is a new method that shows to be effective and efficient. It represents a linear function behavior to summation of network's linear functions to be same as the perception despite of the layers' number. A nonlinear activation function is used in order to cover the probability of getting a nonlinear outcome. Moreover, modification is needed for adjusting the biases and weights in case the required output couldn't be obtained [36].

- *ResNet-50*

ResNet, short for Residual Networks, is a classic neural network used as a backbone for many computer vision tasks, shown in Figure 15. 50 reflects the layers' numbers, as it has double pooling layers and 48 convolutional layers. The figure shows diverse blocks. It is based on the "skip connection" principle; skipping several layers and meanwhile the input of a layer is the output from the previous layer. As a result, gradient problem could be overcome [39].

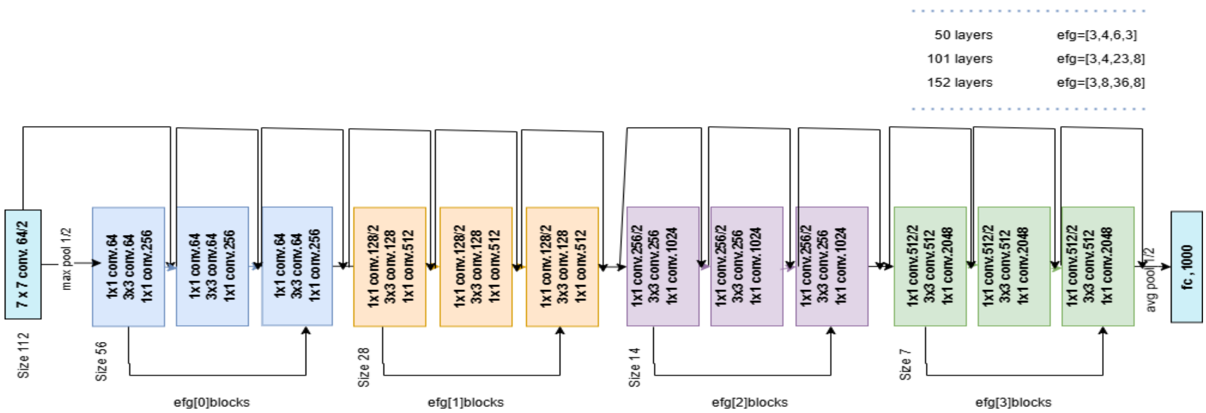


Fig 15. ResNet-50 architecture

- *MobileNetV2*

MobileNetV2 design, as shown in Figure 16, has 17 residual blocks, 53 layers, fully connected layer and an input layer.

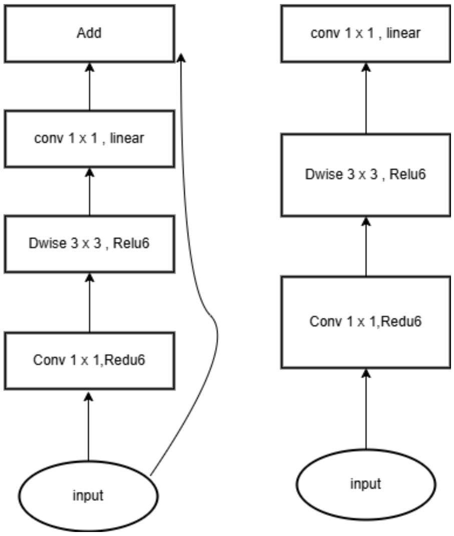


Fig 16. MobileNetV2 architecture

Three layers compose the bottleneck residual block that are two convolution layers, one without an activation function and the other with ReLU6, and depth wise convolutional layer [39].

- *XGBoost*

XGBoost, also known as Extreme Gradient Boosting, is a machine-learning technique used to create Gradient Boosting Decision Trees (GBDT). It effectively manages sparsity patterns and tackles overfitting in complex models. The methodology uses LASSO and Ridge regularization approaches and features built-in cross-validation capabilities for selecting the most suitable number of boosting iterations. The distributed weighted quantile sketch approach is used to determine the optimal number of split points among weighted datasets.[45]

- *LGM Boost*

LGM Boost is an enhanced iteration within the GBDT framework, utilizing histogram-based approaches. It divides continuous eigenvalues into smaller intervals and creates a histogram, identifying the most suitable points for feature segmentation. This technique reduces computational time and memory consumption, making it promising for real-time anemia prediction due to its strong theoretical foundations in data feature extraction and parallel processing, the Light GBM method has promise for real-time anemia prediction.[45]

- *CNN Allnet*

CNN AllNet is a deep CNN that is used for tasks that require image classification. It has 25 convolutional layers divided as follows: 4 convolutional layers in 6 blocks of convolutional layers and one max pooling layer. Both of batch normalization and activation functions follow the convolutional layers. The structure enables input imagers' local features capturing and present model's non-linearity.[46]

- *Efficient Net-B3*

Efficient Net B3, shown in Figure 17, is a member of the family of the Efficient Net models, that present highly accurate outputs and at the same time maintain computational resources. B0 and B1 variants are smaller than B3 variant; it consists of 12.2 million parameters. Diverse methods are utilized in Efficient Net B3in order to attain good level of performance, for example: for model depth, width and resolution balancing, it utilizes compound scaling. "RandAugment" is a novel training method that is being used that randomly augments the data for generalization enhancement.[46]

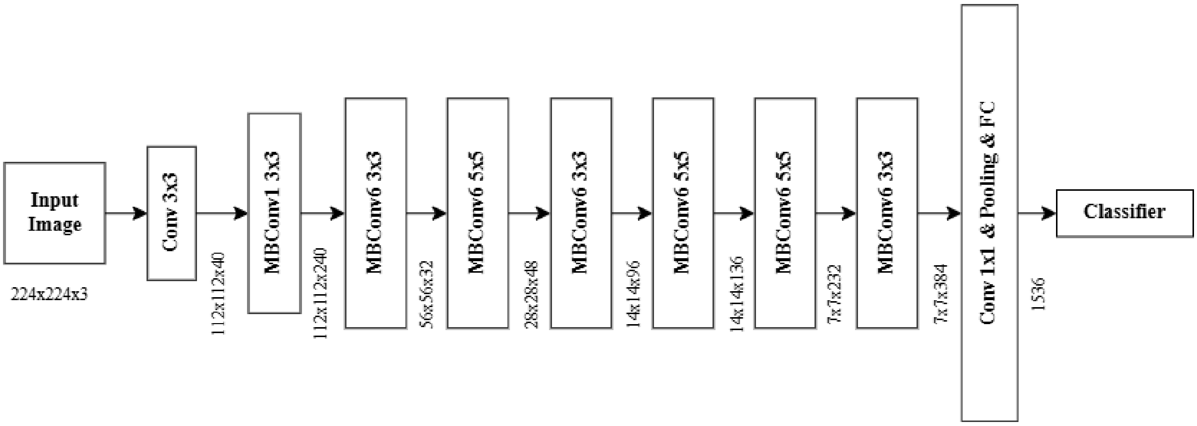


Fig 17. Efficient Net-B3 architecture

- *Dense Net 121*

The DenseBlock, shown in Figure 18, uses equal-size feature maps that comprise connected layers. Three components are used in the nonlinear DenseBlock that are: 3 × 3 convolution function + ReLU + BN. The features of the output image are decided by different layers' DenseBlocks convolution. The addition of the layer of input feature map increases the entire layers numbers. Another layer of bottleneck is introduced in case of big input, this is done by adding to the core structure a 1 × 1 convolution which leads to the final structure of the DenseNet-B. Therefore, the computational proficiency is enhanced as a result of the reduction of features numbers.[46]

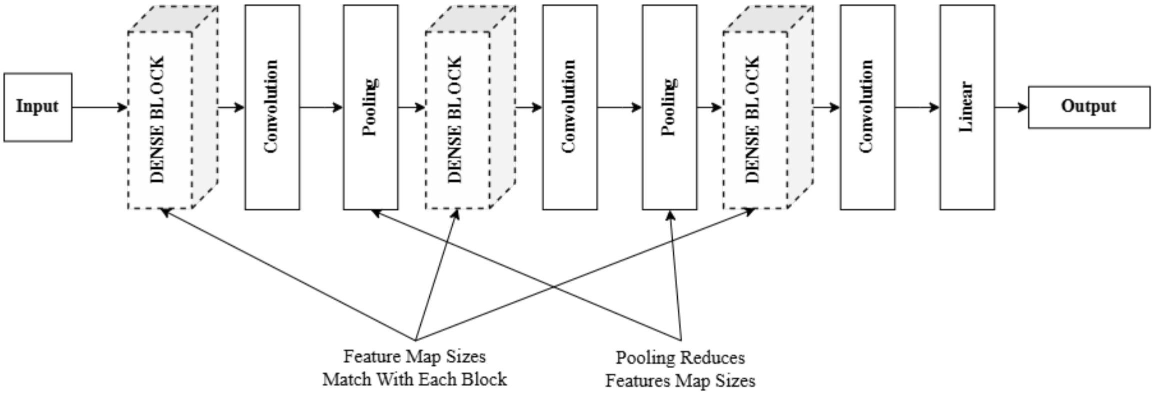


Fig 18. Dense Net 121 architecture

3.3.2.2. Anemia Detection Regions

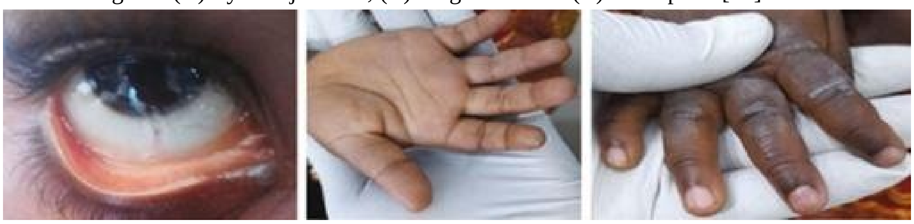
In this subsection different anemia detection body regions that were demonstrated in the selected papers included in the review are discussed. They are fingernails, eye conjunctiva and hand palm. Figures 19, 20 and 21 show anemia detection regions for different cases.

(A) (B) (C)

Fig. 19: (A) Eye conjunctiva, (B) Fingernails and (C) Hand palm [12]

(A) (B) (C)

Fig. 20: (A) Eye conjunctiva, (B) Fingernails and (C) Hand palm [12]



(A) (B) (C)

Fig. 21: (A) Eye conjunctiva, (B) Fingernails and (C) Hand palm [12]

- *Fingernails*

Papers demonstrated several preparation steps before the fingernail can be used for noninvasive detection of anemia. All possible causes of contamination should be eliminated during the preparation of the samples of the fingernails. All kinds of nails cosmetics should be removed before starting the process of nail sampling. Moreover, it is required too to avoid contamination while cutting the nails before being placed in a small box for samples. Such contamination could be from scissors or other tools that may have lost some parts during the process of nail cut. Contamination because of stainless steel is a problem as its magnetic characteristics are weak. Special types of tools to cut the nails can be utilized to avoid such problems.

Generally, the proposed concept of using fingernails is innovative in the next facets: 1) type of non-invasively detection, 2) On the spot screening, 3) Addresses present shortcomings of screening iron deficiency anemia patients around the world, and 4) Can be operated by a technician [13].The developed systems for disease diagnosis using nail image analysis has shown promising accuracy, incorporating image acquisition, processing, and disease prediction. With strict input image standards ensuring optimal analysis conditions, the system’s performance metrics indicate effectiveness in disease detection. Compared to invasive methods, it presents a reliable noninvasive alternative validated against clinical data. [15].

- *Eye Conjunctiva*

When Hb reading is below a specific threshold value, iron deficiency exists. It is known as RBC deficiency. Physicians or medical officers are responsible for examining the eye conjunctiva in order to diagnose IDA. Different levels of blood iron in the vessels can be clearly reflected in the eye conjunctiva. Therefore, eye conjunctiva images are being used for the detection of anemia non-invasively using different AI algorithms. There are several papers presented for the detection of anemia non-invasively using the eye conjunctiva such as [43]. This is achieved by detecting the pallor level which shows effectively reflecting the anemic patients. This is achieved mainly by the physician or medical officer who observes this part of the eye lid and records the level of paleness. This method can be mimicked and applied using AI.

- *Hand Palm*

The hand palm images have proved to be an efficient body region in anemia detection as proved in [11]. When different images were captured from the same patients, images of hand palm presented higher accuracy than fingernail images and eye conjunctiva images when they were utilized for anemia detection in 2months-5years children. Furthermore, this body part can easily be observed when compared to the eye conjunctiva that is very hard body part for observation especially for youngsters as there is a risk of moving while observation which may lead to eye hurt as a result of the physician’s finger enter it. [20]

It is well known that large size datasets are needed for training the model to achieve highly accurate model. This is because the overfitting problem can be resulted from too few samples in dataset which means dataset of a small size [39]. As a result of the seldomness of anemia datasets, applying augmentation on the available images was accomplished to enlarge the number of samples per dataset to be ready for different operations in the model. Image augmentation consists of several operations such as translation, shift, flip and rotation. Table 1 shows a sample from cases used in an article and Figure 16 illustrates a sample of eye conjunctiva, fingernails and hand palm after segmenting the Region Of Interest (ROI) [12]

Table 1. A sample of used image dataset to non-invasive anemia detection [12]

Image ID	Hb Level	Age	Gender	Remarks
Image001	8.9	2	Male	Anemic
Image002	12	5	Male	Non-Anemic
Image003	12	4	Female	Non-Anemic
Image004	12	4	Male	Non-Anemic
Image005	9.9	5	Male	Anemic
Image006	12	1	Female	Non-Anemic
Image007	12	1	Male	Non-Anemic
Image008	12.5	3	Female	Non-Anemic
Image009	9.9	4	Male	Anemic

Figure 22 illustrates some images that were segmented where(A) are patients suffering from anemia and (B) are images healthy humans. (i), (ii) and (iii) are as follows: eye conjunctive, conjunctiva of the eyes, the fingernails, and the hand palm [12].

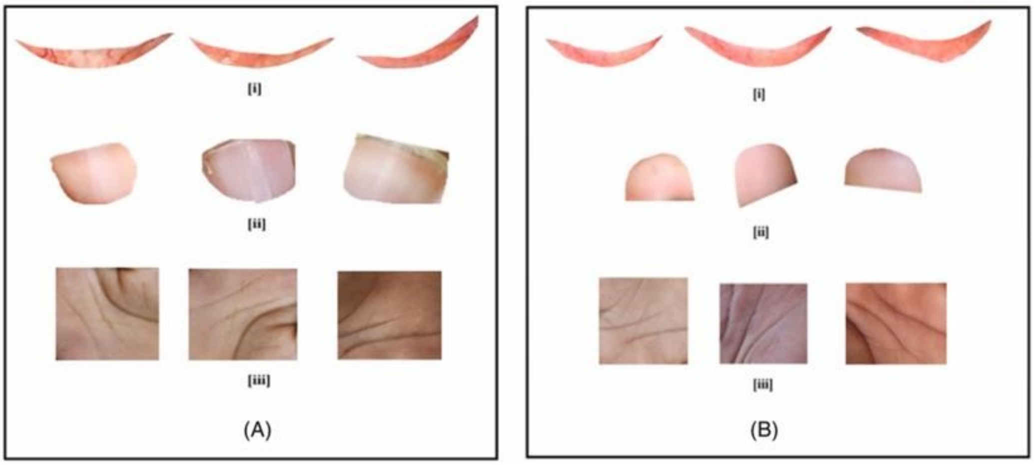


Fig. 22. Segmented ROIs [12]

3.4. Comparative Analysis

A comparative analysis is conducted between the studies involved in the review according to different performance metrics that are described in equations 15-19.

In order for performance evaluation for different AI models, acquired findings were assessed using different evaluation matrices [12].

Accuracy presents the fraction of instances that were predicted correctly amongst the overall instances, it reflects the wellness of the model's performance. It can be mathematically described as in equation 15 [44]:

$$Accuracy = \frac{TP + TN}{TP + FN + FP + FN} \times 100 \quad (15)$$

Sensitivity, Recall, or the true positive rate, all these terms are alternatively utilized. It evaluates the fraction of positive instances that were predicted correctly amongst the overall actual positive instances. It reflects the capability of the model to detect positive instances. It can be mathematically described as in equation 16 [44]:

$$Recall = \frac{TP}{TP + FN} \quad (16)$$

Precision evaluates the fraction of positive instances that were predicted correctly amongst the overall predicted positive instances. It reflects the positive prediction quality. It can be mathematically described as in equation 17 [44]:

$$Precision = \frac{TP}{TP + FP} \quad (17)$$

The F1 score evaluates the performance of the model, the F1 score is proper in case there is an inequality among different instances; the positive and negative ones [44].

$$F1\ Score = \frac{2TP}{2TP+FP+FN} \quad (18)$$

The ROC curve is used to evaluate the equilibrium between accuracy and sensitivity. The area remaining below the ROC curve, known as the Area Under the Curve (AUC), is defined as the ROC score. The ROC curve is plotted depending on the changing classification threshold values of true positives as a function of false positives. A ROC score of ''100'' signifies that the positives are separated from the negatives in an excellent way. A ROC score of ''0'' means that no positives are found, The AUC is calculated as [38]:

$$AUC = \frac{TP}{TP+FN} \quad (19)$$

where TP is True Positive, TN is True Negative, FP is False Positive, and FN is False Negative [12, 47, 50,51].

Table 2 depicts the results of the comparative analysis. Paper [11] that utilized Naïve Bayes AI model introduced the best detection accuracy result of 99.96% when applied on the hand palm images as well as F1 score of 99.97%, AUC of 99.98%, precision of 99.97% and Recall of 99.93%

Table 2. Comparative analysis results

Reference	Region	Algorithm	Performance Measurements %				
			Accuracy	F1	AUC	Precision	Recall
Elec.'20[1]	Conjunctiva	SVM	84	-	-	43	-
		Decision Tree	95	-	-	-	-
		ANN	92	-	-	-	-
Healthcare.'23[4]	Conjunctiva	ELM	99.21	98.84	-	99.30	-
Int. Journal of CS and IT.'23[5]	Conjunctiva	Logistic Regression	80.7	84.8	78.8	83.4	86.2
		Naïve Bayes	90.7	92.1	91.6	96.9	87.8
		Decision Tree	97.2	97.8	94.70	97.5	98.1
		ANN	96.1	96.9	95.9	97	96.7
		SVM	95.1	96	95.5	98	94
		Random Forest	98.4	98.5	97.9	98.1	98.8
Informatics in medicine unlocked.'24[6]	Conjunctiva	CNN	98.45	97.63	99.93	97.64	97.63
		Naïve Bayes	94.94	92.24	97.74	92.64	91.84
		Decision Tree	97.32	96.02	94.70	93.67	98.49
		k-NN	97.96	96.86	99.86	97.60	96.13
		SVM	89.45	84.53	92.16	81.34	87.98
BioData Mining.'23[11].	Palm	CNN	99.92	99.89	99.95	99.79	99.98
		Naïve Bayes	99.96	99.97	99.98	99.97	99.93
		Decision Tree	99.29	98.97	99.38	98.77	99.18
		k-NN	99.92	99.89	99.98	99.79	99.92
		SVM	96.34	94.59	98.97	95.99	93.23
John Wiley & Sons Ltd.'23[12]	Conjunctiva	CNN	98.45	97.63	99.93	97.64	97.63
		Naïve Bayes	94.94	92.24	97.74	92.64	91.84
		Decision Tree	97.32	96.02	97.70	93.67	98.49
		k-NN	97.96	96.86	99.86	97.60	96.13
		SVM	89.45	84.53	92.16	81.34	87.98
	Fingernails	CNN	98.33	97.54	99.93	97.64	97.44
		Naïve Bayes	94.94	92.35	98.01	91.96	92.75
		Decision Tree	97.18	95.61	97.59	98.41	92.96
		k-NN	97.89	96.82	99.83	96.21	97.44
		SVM	92.69	88.62	97.08	91.01	86.35
	Palm	CNN	99.12	99.89	99.95	99.79	99.98
		Naïve Bayes	98.96	99.97	99.98	99.97	99.93
		Decision Tree	98.29	98.97	99.38	98.77	99.18
		k-NN	98.92	99.98	99.98	99.79	99.92
		SVM	95.34	94.59	98.97	95.99	93.23
Int. Journal of Imaging Systems and Technology [19]	Conjunctiva	ANN	97.00	-	-	-	99.21
Medicine in Novel Technology and Devices.'23[20].	Palm	Random Forest	99.53	99.61	-	100	-
		SVM	81.80	80.72	-	84.24	-
		Naïve Bayes	78.16	74.13	-	73.09	-
		ANN	74.45	75.83	-	92.71	-
		Decision Tree	99.20	99.35	-	100	-
Medicine in Novel Technology and Devices.'23[21].	Conjunctiva	ResNet50	84.79	83.7	83.5	85.2	83
		DenseNet121	79.58	78.6	79.3	79	78.8
Frontiers in Public Health.'22 [36]	Conjunctiva	MobileNetV2	80.91	-	-	-	-
		ResNet50	82.08	-	-	-	-
		DenseNet121	81.14	-	-	-	-
		EfficientNetB3	78.31	-	-	-	-

Jurnal Teknik Informatika.’22 [39]	Conjunctiva	AlexNet	89.93	-	-	-	-
		ResNet-50	97.94	-	-	-	-
		MobileNetV2	97.19	-	-	-	-
Int. journal on recent and innovation trends in computing and communication.’23 [44]	Palm	Logistic Regression	92.36	95.19	-	96.19	95.63
		Decision Tree	95.62	98.01	-	98.60	97.92
		Random Forest	91.43	94.98	-	94.36	95.09
		SVM	97.06	97.67	-	97.62	98.19
		Naïve Bayes	93.16	96.31	-	95.65	94.97
		k-NN	94.67	95.34	-	96.49	96.75
		AlexNet	86.97	88.93	-	90.71	89.67
IEEE Access.’24 [45]	Palm	Logistic Regression	74	73.8	-	73.6	74.2
		Decision Tree	80	79.8	-	79.8	80
		XGBoost	86	85.4	-	85.2	85.6
		Random Forest	87	86.8	-	87	87.2
		LGM Boost	91	90.6	-	90.8	90.8
Visual Computing for Industry Biomedicine and Art.’24[46]	Palm	EfficientNetB3	91.2	91.2	-	93.5	89.5
		Dense net 121	94.4	94.4	-	96.4	92.5
		CNN Allnet	96.8	96.8	-	97.7	95.9
Procedia computer science.’24 [47]	Conjunctiva	SVM	91	-	-	-	-
		Mobile Net V2	89	-	-	-	-
		Mobile Net V2 + SVM	93	-	-	-	-
Pattern Recognition and Image Analysis.’19[48]	Conjunctiva	SVM	78.9	-	-	-	-
		k-NN	90.26	-	-	-	-
Biomedical Signal Processing and Control.’24 [49]	Palm	CNN	96.296	-	-	-	94.44

3.5. Datasets Characteristics

Table 3 shows the characteristics of different datasets that were used throughout the reviewed articles. While some articles were concerned with conjunctiva only to be ROI to detect anemia non-invasively, these papers are [6,21], a paper used three different ROI that are fingernails, hand palm and conjunctiva for anemia diagnosis that is [11]. The number of participants were 711, 476 and 218 in articles [6,11 and 21], respectively. Two of them applied their models on participants of the higher age group (from 6-60 and from 19-88) [6,21] and one applied the model to children under 6 years of age [11]. The diagnosis of the cases before being used in the models were as follows: 425 anemic, 289 non-anemic [6], 272 people have anemia while 204 are in good condition [11] and 96 patients suffer from anemia and 122 are healthy people [21].

Table 3. Datasets Characteristics

Dataset	Detection Region	Participants	Age group	Anemic	Non-Anemic
Informatics in medicine unlocked.’24[6].	Conjunctiva	711	6-60	425	286
BioData Mining.’23[11].	Fingernails, Palm, Conjunctiva	476	Children under 6-years	272	204
Medicine in Novel Technology and Devices.’23[21].	Conjunctiva	218	19-88	96	122

3.6. Challenges and limitations of non-invasive anemia detection

Due to the time consumption and pain caused to individuals as a result of blood sample extraction, and costly nature of traditional invasive detection methods, some studies have turned to develop non-invasive prediction methods utilizing the patients' body parts images [11]. Despite the advantages of the non-invasive techniques like the speed of the detection the relatively high accuracy, the lack of need for trained personnel and infrastructure to run the test, it still has some challenges.

- In most of the articles, authors struggled with the limited number of images in datasets. For example, in [46] researchers stated that the most commonly faced limitation is the size of dataset required to train the ai models. However, the publicly accessible datasets are very limited, due to the ethical considerations like the patient's privacy, data protection and generalizing the models to new data to avoid the possibility of bias proved to be a complex task. Moreover, authors of [6] added that anemia is a complex disease, and it can have a variety of symptoms and causes depending of the severity of the disease and the individuals affected by it. Thus, AI algorithms need larger datasets to accurately detect anemia in individuals.
- The individual limitations of different ML models used in reviewed papers. For instance, the SVM algorithm dependance on fixed kernel functions and being slow when training large datasets as it requires high computational complexity. Moreover, Naïve Bayes' assumption that given features are independent, which is not always true. Some of the deep learning models limitations like the CNNs lack of interpretability, dependencies in sequential data and their low ability to deal with unseen data [6].
- Challenges associated with the invasive and non-invasive detection techniques compared factors such as data collection sites, bio-signal processing techniques, theoretical foundations, photoplethysmogram signal analysis, machine-learning algorithms, and prediction models for Hb level calculation. [15]
- The efficiency and speed of model training and evaluation can be affected by the availability of limited hardware resources, such as GPUs and memory, which may result in variations in the models' performance. [49]
- Additionally, the complexity of the prediction models used in resource-constrained environments may need to be modified to optimize performance while taking computational limitations consideration, which could lead to unstable levels of accuracy and efficiency [49].
- Non-standardized image poses can cause challenges in image processing and also the noise caused by poor image quality, requiring techniques like segmentation and brightness calibration to enhance image quality, non-standardized image setups cause imbalanced dataset, with limited samples displaying values outside the normal range, impacting the reliability of the models [52].
- In the case of children, some of them had inadequate conjunctiva exposure, which may have resulted from slender conjunctiva or insufficient eyelid retraction, making precise segmentation difficult [53].
- Some non-invasive techniques might not be accurate when using static samples because they can limit

prediction models' ability to generalize because they may fail to consider the wide range of individual variations like in Hb or skin color, which may affect the model's performance over time [53,54].

4. Conclusion & Future Work

Anemia is a highly prevalent disease that is associated with several morbidities. It negatively affects patients' life quality and increases the global cost of healthcare. The most important cause of anemia is iron deficiency that always presents weakness, pallor, dizziness, etc.

This review paper demonstrates the case of employing different image processing and AI algorithms for the purpose of the anemia detection utilizing non-invasive methods using images from different body regions that are eye conjunctiva, fingernails and hand palm. The Invasive methods of detecting anemia have several drawbacks such as being so expensive and time consuming. Moreover, several patients feel discomfort due to pain during the blood sample extraction. Furthermore, some clinicians or nurses are exposed to prick during the blood extraction process. Therefore, migrating to non-invasive anemia detection approach is needed. The articles involved in the review demonstrated several AI models employed for anemia detection non-invasively that are CNN, k-NN, Decision Tree, Naive bayes, SVM, Logistic regression, random forest, AlexNet, ELM, XGBOOST, LGMBoost, RESNet-50, MobileNet20, EfficientNet-B3, Dense Net 121, CNN Allnet, and ANN to be applied on eye conjunctiva, hand palm and fingernail images. A comparative analysis is conducted throughout the review and reveals that palpable hand palm images present the best accuracy among other body region images in iron deficiency anemia detection using the Naïve Biase model. AI models make it more efficient, accurate, cost effective and less time used for anemia detection, the lack of need for trained personnel and infrastructure to run the test. Despite the advantages of the non-invasive detection method, it still has some challenges such as the limited number of images in databases that negatively affect the models' accuracy and cause overfitting. Regarding the future work, researchers can focus on exploring additional non-invasive detection methods and improving the accuracy of the proposed AI models by adjusting different lightings, conveying diverse image setups, and collecting large and varied datasets from different genders, ages, ethnicities would help train the models to increase their accuracy. Developing hybrid models or stacking old models to try and overcome their limitations. The collection of large and diverse datasets from different genders, ages, ethnicities would help train the models to increase their performance and accuracy by collaborating with health care professionals and facilities like clinics and hospitals. Moreover, enhancing different image pre-processing techniques such as segmentation and feature extraction process, and exploring other body regions for non-invasively methods of anemia detection, other than the hand palm, the eye conjunctiva and the fingernails. Moreover, developing a mobile application for wider usage of the proposed non-invasive anemia detection models and making them easily accessible in the poor areas that need this approach of anemia detection, and making it user friendly. Replacing traditional anemia detection process that depends on extracting blood samples by developing and installing portable and affordable hardware devices that can detect the anemia non-invasively using one of the proposed AI models in this review paper to be used especially in rural areas that suffer from lack of trained personnel or proper infrastructure to perform the traditional anemia detection process.

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