A Review on Diabetic Retinopathy Disease Detection and Classification using Image Processing Techniques

Valarmathi S[1], Dr. R. Vijayabhanu[2]

[1]Research Scholar, Department of Computer Science, Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore, Tamil Nadu, India
[2]Assistant Professor, Department of Computer Science, Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore, Tamil Nadu, India

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Abstract - *In this era, diabetes is the most widely found chronic disease present in people of various age groups having insufficient insulin production, which produces high blood sugar. Diabetes, when left undiagnosed, may lead to the development of various diseases across the body. Diabetic Retinopathy (DR) is an eye disease caused by diabetes, which results in damaged retinal blood vessels and may lead to vision loss. Many computer-aided diagnostics systems have been developed in the past, which used traditional techniques where handcrafted features are used. With the advent of Deep Learning, especially in medical image analysis, more accurate and robust results are produced, as it performs feature extraction task automatically. Convolutional Neural Networks (CNNs) are the most commonly used deep learning method in medical image classification. In this paper, various conventional and deep learning-based diabetic retinopathy disease detection and classification methods are reviewed and analyzed to provide a clear insight and future directions.*

Key Words: **Computer-aided diagnostic systems, Convolutional Neural Network (CNN), Deep Learning, Diabetes, Diabetic Retinopathy, Medical image processing**

1. INTRODUCTION

Diabetes is one of the highly prevalent diseases globally, causing deleterious effects on various organs of the body, which exhibit micro and macrovascular changes. Almost 382 million of the human population was found to be diagnosed with diabetes, and it can scale up to 592 million as per global prediction. Prolonged diabetes may lead to several eye complications such as Diabetic Retinopathy (DR), Glaucoma, Diabetic macular edema, Cataracts, and so on. Most diabetic patients are highly susceptible to Diabetic Retinopathy that harms the retinal blood vessels, which may lead to complete vision loss. Through early disease detection and proper screening, nearly 90% of diabetic patients can be diagnosed, and the disease progression can be minimized by extricating the future consequences. The paramount problem lies in the fact that DR does not uncover typical symptoms until an extreme stage is attained. Hence, periodic eye examinations and regular check-up is entertained to reduce complications. However, a human inspection of retinal features and morphological variations in the fundus images are monotonous and demanding tasks. To overcome this drawback, several automated computer-aided diagnostic systems were evolved in recent times, which act as an assistant for the ophthalmologists to examine the retinal abnormalities.

This paper is organized as: Section 2 provides a brief note on medical image processing, and imaging modalities, Section 3 and its subsections describe Diabetic Retinopathy, classifications, and its risk factors. In Section 4, the literature review has been done separately using traditional and deep learning-based approaches to understand existing works better. Finally, Section V concludes the paper with the examined inferences gained throughout the study.

2. MEDICAL IMAGE PROCESSING

In patients' history analysis and future progress prediction, Electronic Health Records (EHR) assists the physicians by maintaining the medical records digitally. Some of the common operations performed on medical images are preprocessing (image enhancement, noise removal, and so on), segmentation, localization, detection, feature extraction, classification, visualization, and much more. More specifically, in our DR study, some of the operations can be listed as follows: detecting microaneurysms, and hemorrhages, locating optic disc and cup, blood vessel segmentation, optic disc, and cup segmentation, classifying the DR fundus images into severity-based stages and so on. Nowadays, medical imaging modalities are highly equipped with robust digital sensors to collect more accurate data quickly. Some of them are Computer Tomography (CT), Ultrasonography, Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), Retinal photography, Dermoscopy, Radiography, Angiography, and Mammography. The ever-increasing need for such imaging modalities assists radiologists in analyzing and producing better results quickly.

3. DIABETIC RETINOPATHY

Diabetic patients worldwide profoundly suffer from Diabetic Retinopathy over time, which may not exhibit any prior visible symptoms and may even lead to blindness. DR affects the vision and damages the blood vessels around the retinal region. DR risk factors and its classifications are discussed below to have a better understanding of the disease. The Healthy retina and DR-affected retina are shown in Fig -1 and Fig -2 respectively.

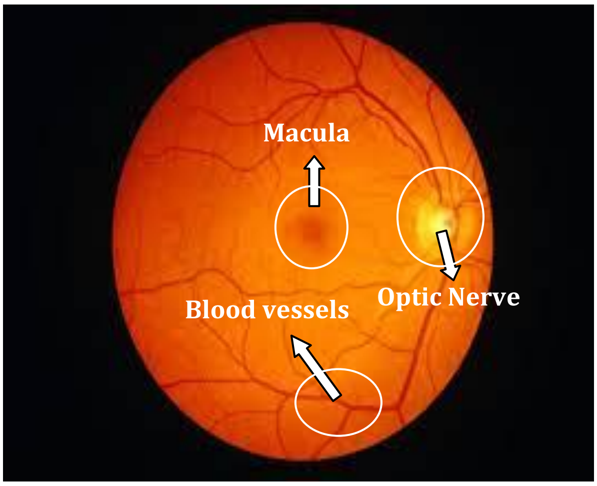

Fig -1: Healthy retina

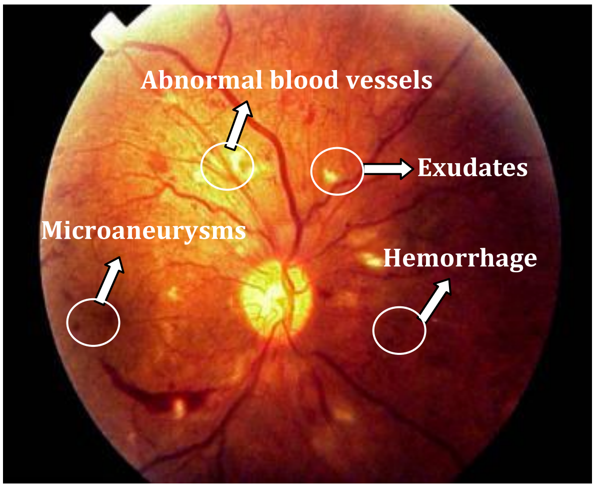

Fig -2: DR-affected retina

3.1 Risk factors

Diabetes – Period

The Diabetic period is one of the most decisive and primary risk factors of Diabetic Retinopathy. Table -1 encloses the DR prevalence proportion in both Type I and II diabetic patients.

Table -1: DR prevalence proportion in Type I and II diabetic patients

Diabetes time span	Type I Diabetics	Type II Diabetics
After 10 years	20%	25%
After 20 years	90%	60%
After 30 years	95%	95%

According to global reports, type I diabetic patients are highly susceptible to Diabetic Retinopathy than type II patients in common. More specifically, type I diabetic patients are much exposed to Proliferative Diabetic Retinopathy (PDR), whereas Diabetic macular edema found highly in type II patients.

Poor metabolic control and Heredity

Poor metabolic control may lead to DR disease development and progression in diabetic patients. Diabetic Retinopathy is a genetic disorder that produces a great impact on the eye when left untreated.

Pregnancy and Hypertension

The retinal features which get altered or changed during the pregnancy period are called Gestational diabetes. The other risk factors are hypertension, smoking, obesity, and anemia, which may lead to significant morphological changes.

3.2 DR Classification

Based on the morphological changes in the fundus images, Diabetic Retinopathy has been classified into two types, Non-proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR). The NPDR and PDR features and risk levels are described in the below sections.

3.2.1 DR Features

Non-proliferative Diabetic Retinopathy (NPDR) occurs as an early-stage DR retinal disease which shows the following symptoms,

- **Microaneurysms (MA)** are mostly found in the macular region, which appears as red spots whose size is less than 125µm with sharp margins and is one of the earliest signs of DR.
- **Hemorrhages (HM)** appear to have larger spots whose size is greater than 125µm. Blot HM and Superficial HM are the hemorrhage types that occur due to capillary leakages.
- **Hard exudates** appear to have bright yellow spots with sharp margins in the macular region due to the plasma leakage.
- **Cotton wool spots,** also called **Soft exudates,** appear to have white spots on the retinal area due to the swollen nerve fibre.
- **MA** and **HM** are the red lesions, whereas **Hard exudates** and **Soft exudates** are the bright lesions found in the retinal area.

Proliferative Diabetic Retinopathy (PDR) occurs as an advanced stage DR retinal disease which shows the following symptoms,

- **Neovascularization** mainly occurs in the PDR stage, where new abnormal blood vessels are formed at the optic disc or elsewhere in the retinal region.
- **Vitreous hemorrhage -** The abnormal retinal blood vessels may proliferate or spread within or around the vitreous body

3.2.2 DR Risk levels

According to the Early Treatment Diabetic Retinopathy Study (ETDRS), the Diabetic Retinopathy (DR) risk levels are listed in Table -2.

Table -2: Diabetic Retinopathy risk levels

DR Risk level	Lesions
No DR	○ No lesions
Mild NPDR	○ Presence of MA
Moderate NPDR	○ Presence of MA and HM ○ Presence of Cotton wool spots and Exudates
Severe NPDR	Any of the symptoms, ○ Venous beading in 2 quadrants ○ Presence of MA and extensive HM in 4quadrants ○ Intraretinal microvascular abnormalities in 1 quadrant
PDR	○ Neovascularization ○ Presence of preretinal & vitreous HM

4. LITERATURE REVIEW

4.1 Traditional DR Detection approach

Chandrashekar [1] proposed a work using morphological methods for the retinal vessels extraction on the retinal fundus images. Jaspreet and Sinha [2] proposed a segmentation method that uses morphological filters for segmenting blood vessels. No effective improvement in the performance on increasing the filter bank counts; instead it increases the convolution operation, which is a time-consuming task. Hussain et al. [3] proposed a method that uses adaptive thresholding for exudates detection and eliminates artifacts from the exudates; the retinal structures are used in classification. The proposed method did not cover all the DR signs; it needs to be explored. Jiang and Mojon [4] proposed a method, adaptive thresholding on verification-based multi-threshold probing approach. With global thresholding, the blood vessels cannot be segmented due to the image gradients. So, image probing with various threshold values were used to extract the thresholded image. Sanchez et al. [5] proposed a mixture model that separates the exudates from the image background, and edge detection methods are used to separate hard and soft exudates.

Jonathan et al. [6] used multiple classifiers for the retinal image classification. To distinguish the blood vessels, microaneurysms, and exudates, segmentation was carried out on fundus images. The segmented region, textural features, and other features obtained from GLCM were given to the classifiers to classify the normal and abnormal images. The detection system has achieved 92% on normal images and 91% on abnormal images. Gerald Liew [7] used a statistical approach that showed the association of retinal vascular signs and highlighted both qualitative and quantitative evaluation of retinal vasculature. This proposed system needs trained assistance in the identification of blood vessels. Reza et al. [8] used a marker controlled based watershed segmentation method, which detects the exudates and optic disk. Before that, average filtering and contrast enhancement has been applied to remove artifacts. Hoover & Goldbaum [9] proposed a fuzzy-based voting system that detects the optic disk location where many feature elements overlap. Li and Chutatape [10] used an active shape model, which is a model-based approach to extract the vasculature parts based on the Optic disk location. The extracted data was used to discover the central macular region.

Gardener et al. [11] used an Artificial Neural Network (ANN) to find different features such as exudates, blood vessels, and hemorrhages with 93.1%, 91.7%, and 73.8% of accuracy. Yun et al. [12] proposed an automatic diabetic retinopathy classification system that classifies mild, moderate, and severe non-proliferative diabetic retinopathy and proliferative diabetic retinopathy and achieved an accuracy of 72% which extracts six features. In general, the traditional approach for DR detection and classification can be made, as shown in Fig -3. Initially, the data can be collected, preprocessed, image segmentation can be performed to segment the essential part, image features are extracted manually, and classification can be done separately using binary or multi-class classifiers.

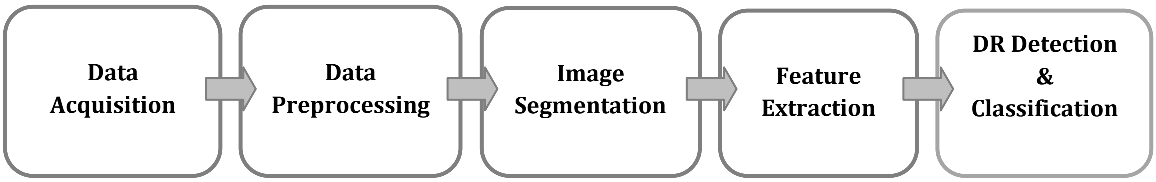

Fig -3: DR detection and classification process using traditional method

4.2 Deep Learning based DR Detection Approach

Deep Learning (DL) has become a robust tool that acts as a part of machine learning and an optimal technique which can replace machine learning in most areas. Deep Learning model has a hierarchical based architecture which consists of a multilayered structure. Predominantly, in medical image analysis, DL plays a unique role in medical image classification, localization, segmenting essential data, and detection. Recently, in Diabetic Retinopathy disease detection and classification, DL provides impressive results with various methods. Some of the DL-based methods are Convolutional Neural Networks (CNN), Deep Boltzmann Machines (DBM), Auto encoders, Deep Neural Networks (DNN), Recurrent Neural Networks (RNN), Deep Belief Networks (DBN), Generative Adversarial Networks (GAN) and sparse coding. An increase in the number of training data increases the model performance since many low, and high-level features are automatically extracted and learned from the training data.

Convolutional Neural Networks (CNNs) are universally used by many researchers in medical image analysis than other DL-based methods. The CNN architecture consists of three common layers: convolutional layers, pooling layers, and fully connected layers. According to the researcher's vision and requirement, CNNs size, the number of layers, and filter count vary. In the convolutional layers, various filters combine to extract the image features to produce feature maps. Next, in the pooling layers, those feature maps dimensions are reduced mostly using the average or max-pooling technique. After pooling layers, fully connected layers are used, which describes the overall image feature set. Finally, the classification task is accomplished by one of the two activation functions, sigmoid for binary classification and softmax for multi-classification, respectively. Some of the pre-trained CNN architectures available on the ImageNet dataset are LeNet, AlexNet, GoogLeNet, VGGNet, and ResNet. These pre-trained architectures are used to speed up the training process with transfer learning strategies such as fine-tuning some of the middle layers or fully connected layers, or in some cases, the whole pre-trained model is trained.

In general, the DL-based DR detection and classification can be done, as shown in Fig -4. Initially, the data can be collected, preprocessed to enhance the image quality, augmentation can be done if necessary when the image samples are less. Then, it can be fed into the DL model to extract image features and classify them according to the severity levels.

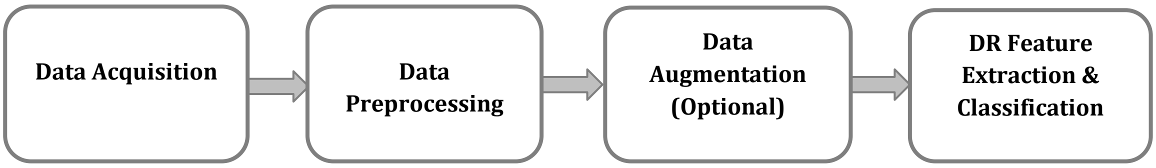

Fig -4: DR detection and classification process using DL-based method

Many DL-based automatic diabetic retinopathy detection systems were developed, and the classification method differs from researcher to researcher. Some of the classification methods used in literature are Binary and multi-level classifications, Vessels-based classification, and Lesion-based classification.

4.2.1 Binary and multi-level classification

In diabetic retinopathy disease detection, various studies have been made on different classification methods. In binary classification, the diabetic retinopathy disease has been classified into two classes only. As per studies, the two classes can be normal image/DR image and Referable DR/Non-referable DR. In multi-level classification, the diabetic retinopathy disease has been classified into many classes as per researchers' vision.

Binary classification

Quellec et al. [13] proposed an automated detection method where three CNNs (AlexNet and two other networks) were used to detect microaneurysms, hemorrhages, soft and hard exudates from three different datasets, Kaggle, DiaretDB1and E-ophtha (private). The fundus images were resized, cropped, normalized, augmented, and the Gaussian filter was applied in the preprocessing phase. The disease was classified into two classes, referable and non-referable DR, and produced a ROC value of 0.954 and 0.949 in Kaggle and E-ophtha, respectively.

Jiang et al. [14] proposed a model where three pre-trained CNNs (Inception-v3, ResNet152, and Inception-ResNet-v2) were used to classify the dataset as referable diabetic retinopathy or non-referable diabetic retinopathy. Before CNN training, the images were resized, enhanced and augmented, and then the models were integrated using Adaboost technique. Further to update the network weights, Adam optimizer was used and the system achieved 88.21% accuracy and AUC value of 0.946.

Zago et al. [15] proposed a method where two CNNs (pre-trained VGG16 and a CNN) were used to detect Diabetic Retinopathy or non-diabetic retinopathy images based on the red lesion patches probability. This model was trained on the DIARETDB1 dataset, and it was tested on the few datasets: IDRiD, Messidor, Messidor-2, DDR, DIARETDB0, and Kaggle. The model achieved the best results on the Messidor dataset with a sensitivity value of 0.94 and an AUC value of 0.912.

Multi-level classification

Pratt et al. [16] proposed a method where a CNN was used with ten convolutional layers, eight max-pooling layers, three fully connected layers, and a softmax classifier was used to classify the Kaggle dataset images into five classes according to the DR severity levels. During the preprocessing phase, the images are color normalized, resized, and to reduce overfitting, L2 regularization and dropout techniques were used. The system produced a specificity of 95%, an accuracy of 75%, and a sensitivity of 30%.

Gulshan et al. [17] proposed a method where 10 CNNs (pre-trained Inception-v3) were trained to detect Diabetic macular edema (DME) and Diabetic retinopathy. Eyepacs-1 and Messidor-2 datasets were used to test the CNN model. The dataset images were initially normalized, resized and fed into the CNN model to classify the images into referable DME, moderate/worse DR, severe/worse DR, or fully gradable DR. The model produced a specificity of 93% in two of the datasets taken and sensitivity of 97.5% and 96.1% in eyepacs-1 and Messidor-2 datasets respectively.

Wang et al. [18] used three separate CNNs (pre-trained VGG16, AlexNet, and Inception-v3) to detect the 5 stages in DR using the Kaggle dataset and compared the performance of the individual CNNs. The dataset images were resized to different sizes for all three pre-trained CNN models and achieved an accuracy of 63.23%, 50.03%, and 37.43% in Inception-v3, VGG16, and AlexNet respectively. Some of the merits and demerits of the multi-level DR classification methods are presented in Table - 3.

Table -3: Merits and Demerits of Multi-level DR classification methods

DL Technique	Dataset	Merits	Demerits
CNN [19]	Messidor-2 (1748 images)	○ IDX-DR device was integrated with a CNN for DR detection and classification	○ They considered mild DR images as no DR ○ The 5 DR severity levels were not examined
1. Back propagation Neural Network (BPNN) 2. Deep Neural Network (DNN) 3. CNN (pre-trained VGG16) [20]	Kaggle (2000 images)	○ The dataset images were preprocessed by detecting edges, applying median filter, and binary conversion and so on ○ The result shows DNN surpasses the CNN and BPNN	○ For network training, they have not used many images. So, the model could only learn few features ○ They have used only one dataset to assess their work
CNN (AlexNet, ResNet, GoogLeNet, VGGNet) [21]	Kaggle (35,126 images)	○ Transfer learning were used which ultimately reduces the training time ○ The last FC layer and hyperparameter alone was tuned ○ VGGNet achieved best results	○ They have used only one dataset to assess their work ○ No DR lesions were detected
CNN (pre-trained AlexNet) [22]	1. Training - Kaggle 2. Testing – IDRiD	○ The AlexNet and the handcrafted features are integrated	○ They have used only one dataset to assess their work ○ No DR lesions were detected
R-FCN [23]	1. Messidor 2. Private dataset	○ Feature pyramid network and 5 region proposal networks has been added to modify a R-FCN method	○ They have used only one public dataset to assess their work ○ No exudates detected, only HM and MA are detected

4.2.2 Vessels-based classification

To evaluate the retinal disease progression and diagnosis, vessel segmentation is commonly done in detecting various retinal diseases such as Diabetic Retinopathy, Glaucoma, and so on. Once the blood vessels are segmented, the DR lesions can be easily found, which leads to effective DR detection and classification. Some of the research works based on vessel segmentation have been reviewed in this section.

Hua et al. [24] used the DRIVE dataset and extracted the retinal blood vessels. The author used a pre-trained ResNet-101 network to select four feature maps, and it was combined to form a single feature map. The dataset images were augmented before fed into the CNN. Subsequently, the best feature maps were concatenated to provide an accuracy value of 0.951, a sensitivity value of 0.793, AUC value of 0.9732, and a specificity value of 0.9741.

Wu et al. [25] proposed a CNN, which extracts the retinal blood vessels from three of the public datasets: STARE, DRIVE, and CHASE. In the preprocessing stage, the RGB images were converted into grayscale images, normalized, augmented, and the contrast enhancement has been performed using CLAHE. CNN consists of encoder-decoder structure, which contains convolutional, normalization, concatenation, and dropout layers, and skip connections were also made. The system produced an AUC of 98.75%, 98.30%, and 98.94%, and an accuracy of 96.72%, 95.82%, and 96.88% for the STARE, DRIVE, and CHASE datasets respectively.

Oliveira et al. [26] proposed a fully CNN model that extracts the retinal vessels from the following dataset images: DRIVE, STARE, and CHASE_DB1. The dataset images were preprocessed before fed into the CNN. The Stationary Wavelet Transform (SWT) was applied after extracting the green channels and normalizing the dataset images. Then the patches were extracted from the images, and it was augmented before CNN processing. The system produced an AUC value of 0.9821, 0.9905, and 0.9855 in DRIVE, STARE, and CHASE_DB1 datasets, respectively.

4.2.3 Lesion-based classification

To evaluate the DR progression and diagnosis, lesion-based detection methods have been used, and some of the research works have been reviewed in this section.

Chudzik et al. [27] proposed a CNN model where it consists of 18 convolutional layers, batch normalization layers, three max-pooling, and up-sampling layers, and finally, 4 skip connections were made. The author used three datasets: E-ophtha, DIARETDB1, and ROC to detect microaneurysms from the DR images. The dataset images were preprocessed before CNN processing, the green planes are extracted, cropped, resized, and Otsu thresholding has been applied to generate a mask, and morphological functions are utilized to produce a ROC value of 0.355.

Wang et al. [23] proposed a method that detects hard exudate lesions by combining the handcrafted features with the CNN features using the Random Forest classifier in two of the datasets: HEI-MED and E-ophtha. The preprocessing steps involved are cropping, color normalization, morphological operations, and dynamic thresholding have been used to detect the candidates. The CNN was constructed using three convolutional and pooling layers, and to detect the features, one FC layer has been used. The proposed work produced an AUC value of 0.9323 and 0.9644 and a sensitivity of 0.9477and 0.8990 in HEI-MED and E-ophtha datasets, respectively.

Yan et al. [28] proposed a method where two CNN architectures (U-net and improved LeNet) were used to detect Diabetic retinopathy red lesions from the DIARETDB1 dataset images by combining the conventional handcrafted features, and the improved LeNet architecture features using Random forest classifier. In the preprocessing phase, the green channel was cropped, CLAHE has been applied to enhance the contrast, and the noise has been removed by the use of Gaussian filter, and the morphological operations have been performed. The U-net architecture was used to segment blood vessels from the dataset images, and the LeNet architecture has been improved with four convolutional layers, three max-pooling layers, and one fully connected layer to achieve 48.71% of sensitivity, while detecting red lesions. Some of the DL-based DR detection and classification methods are discussed in Table -4.

Table -4: DL-based DR detection and classification methods

DL Technique	Lesion detection	Dataset	Performance Metrics		
			Accuracy	Sensitivity	Specificity
CNN [25]	No	DRIVE (40) STARE (20) **CHASE (28)**	95.82% 96.72% **96.88%**	79.96% 79.63% **80.03%**	98.13% 98.63% **98.80%**
CNN [23]	Red lesion only	Messidor (1200) **Private dataset (9194)**	- **92.95%**	92.59% **99.39%**	96.20% **99.93%**
Deep Residual Network [29]	Exudates only	**HEI-MED (169)** E-ophtha (82)	- -	**0.9255** 0.9227	- -
CNN (Inception-v3, Inception-ResNet-v2, ResNet-152) [14]	No	Private dataset (30244)	88.21%	85.57%	90.85%

Fully CNN [26]	No	DRIVE (40) STARE (20) CHASE_DB1(28)	0.9576 **0.9694** 0.9653	0.8039 **0.8315** 0.7779	0.9804 0.9858 **0.9864**

Inferences

Overall, on comparing the performance and analyzing the results of both traditional and Deep Learning-based methods, the DL-based methods outperform the conventional methods, as discussed in the literature study. On individually reviewing the DL-based methods, Conventional Neural Network (CNN) and its pre-trained architectures have been used by most of the researchers, and it has produced more potential results. However, CNN suffers from different issues; one of them is data annotation, where it requires the ophthalmologists' services to label the retinal fundus images. Class imbalance and overfitting are the other issues which may result in biased prediction. An increase in data increases the performance of the DL-based systems, which may not be possible in all kinds of problems. More research work must be performed on this area to encounter all the above drawbacks and also to increase the robustness and performance of the system.

5. CONCLUSION

Automated DR Disease detection systems remarkably reduce the diagnosis time, cost, and helps as an assistant for ophthalmologists in detecting retinal abnormalities and providing timely treatment. These automated systems play a crucial role in detecting diseases more accurately. Some studies have suggested that while integrating the handcrafted and CNN based features, the performance has been increased. In future, CNN architectures can be integrated to extract more accurate and finer image features which ultimately improve DR detection and classification rate. Initially, in this paper, a brief description was given on medical image processing, Diabetic Retinopathy risk factors and classifications. Conventional and DL-based DR detection methods are discussed, along with their performance metrics. Most of the researchers have used CNN for its efficiency and ability to provide more accurate results, which surpasses the other methods. This review paper discusses the recent works, and the most useful techniques are put forth, which helps the research community in detecting and classifying DR.

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BIOGRAPHIES

Valarmathi S has completed her Master degree in M.Sc. Computer Science and Bachelor degree in B.Sc. Computer Science at Sri Krishna Arts and Science College, Coimbatore in 2019 after which she is undertaking Doctoral Research at Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore. Her research area in computer science includes Image Processing and her current research work is focused on Diabetic Retinopathy Disease Detection and Classification.

Dr. R. Vijayabhanu is an Assistant Professor in the Department of Computer Science. She has completed MCA, M.Phil and Ph.D in Computer Science at Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore. Her thesis is area of Soft computing. She has published 22 papers in International journals and presented five papers at International Conferences.