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Automatic Detection of Diabetic Retinopathy: A Review on Datasets, Methods and Evaluation Metrics

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ABSTRACT Diabetic retinopathy (DR) is a fast-spreading disease across the globe, which is caused by diabetes. The DR may lead the diabetic patients to complete vision loss. In this scenario, early identification of DR is more essential to recover the eyesight and provide help for timely treatment. The detection of DR can be manually performed by ophthalmologists and can also be done by an automated system. In the manual system, analysis and explanation of retinal fundus images need ophthalmologists, which is a time-consuming and very expensive task, but in the automated system, artificial intelligence is used to perform an imperative role in the area of ophthalmology and specifically in the early detection of diabetic retinopathy over the traditional detection approaches. Recently, numerous advanced studies related to the identification of DR have been reported. This paper presents a detailed review of the detection of DR with three major aspects; retinal datasets, DR detection methods, and performance evaluation metrics. Furthermore, this study also covers the author's observations and provides future directions in the field of diabetic retinopathy to overcome the research challenges for the research community.

INDEX TERMS Artificial intelligence, deep learning, diabetic retinopathy, fundus images, machine learning, ophthalmology.

I. INTRODUCTION

The retina is a sphere-shaped structure, composed of a thin layer, located in the backside of an eye. The function of a retina is to transfer the light into the neural signals and coordinate with the brain to process the visual information. The retina is placed beside the optic nerve, and a dark circular part located in the center of the retina is called macula. The fovea is a central part of the macula, which provides a clear vision [1].

All over the world, diabetes is a widespread disease. The diabetic patients between 20 to 74 years old can suffer blindness because of hysterical diabetes and this kind of disease is called diabetic retinopathy [2]. In the human body, retinal tissue, similar to all the other tissues, receives blood supply via the body's vasculature. Additionally, the retinal tissue

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receives the blood through micro blood vessels and needs to retain the blood sugar level with the uninterrupted flow of blood. The abnormal condition of the sugar level in the retinal blood vessels leads to microaneurysms (MAs). MA is an early sign of diabetic retinopathy, which can be considered as a basic element of diabetic retinopathy. The shape of MAs is almost circular with darkish color and tiny in size. Later, the abnormal retinal blood vessels may breakdown into the form of micro vascular networks, which is called retinal neovascularization. Diabetic retinopathy also contains some other abnormalities including cotton wool spots, hemorrhages, exudates which lead to non-reversible blindness and vision impairment.

The international clinical diabetic retinopathy (ICDR) scale is one of the more commonly used clinical scales and consists of a 5-point grade for DR: no, mild, moderate, severe, and proliferative. The ICDR classification used by most of the artificial intelligence (AI) algorithms for DR



FIGURE 1. (a) PDR (b) Severe NPDR (c) Moderate NPDR (d) Mild NPDR (e) Normal Retina [7].

grading and severity [3]. Generally, diabetic retinopathy is divided into two levels; proliferative diabetic retinopathy (PDR) and non-proliferative diabetic retinopathy (NPDR). NPDR is further subdivided into mild, moderate and severe non-proliferative diabetic retinopathy [4]. The standard features of all the types of DR are explained in TABLE 1.

TABLE 1. Types of diabetic retinopathy with its standard features [6].

| | T (DD |
|--|------------------|
| Existence of standard features | Types of DR |
| The new blood vessels formation with all the retinal abnormalities | PDR |
| Retinal abnormal features in four quadrants | Severe NPDR |
| Numerous signs of Hemorrhages, Exudates, and Micro- aneurysms | Moderate NPDR |
| Signs of Micro-aneurysms | Mild NPDR |

NPDR is an abnormal stage of diabetic retinopathy having leakage of blood vessels into the retina. Finally, the retina becomes wet and inflamed. Retinal abnormalities including, hemorrhages, exudates and micro aneurysms can be identified at the stage of NPDR. Hemorrhages are identified with the texture of blood dots on the retina, exudate is a basic sign of DR, soft exudates are exemplified as light yellow or white areas with distracted edges but hard exudates are illustrated as yellow waxy patches in the retina [5]. The existence of exudates in the retinal fundus photographs is one of the most serious causes of DR. MAs are also the early signs of because of retinal vasculature widens. Figure 1 shows the pictorial representation of normal retina and different levels of DR.

In this scenario, early identification of DR may assist the affected person to have timely and proper treatment. According to the survey report, many experts have declared that almost 90% of diabetic patients can be saved by early detection of diabetic retinopathy [8]. The detection of DR can be manually performed by ophthalmologists and also can be done by an automated system. There are some advantages and disadvantages of both manual and automatic detection methods of diabetic retinopathy. The only advantage of the manual DR detection method is that there is no requirement of computer assistance in a manual process, but here it is more important that the ophthalmologist must be an expert in the area of DR detection. Occasionally, the marks of diabetic retinopathy at their early stage are tiny, even can be missed by ophthalmologists. On the other hand, in the area of ophthalmology, artificial intelligence (AI) is performing a vital role to diagnose serious diseases including diabetic retinopathy (DR). The advantages and usefulness of the automated system are much more as compared to the manual system. The detection of diabetic retinopathy through an automated system is much more authentic, reliable, faster, efficient and easier than the manual system. Therefore, automated detection of DR is essential.

Deep learning is the most popular and successful approach in the area of ophthalmology to identify the DR. According to research studies, Kwasigroch et al. [9] introduced an automatic diabetic retinopathy monitoring approach on the basis of deep learning. The performance of the defined method was evaluated by a retinal dataset having 88,000 fundus images. In the presented technique, a special class coding approach was integrated during the training phase of convolutional neural networks. Quadratic weighted kappa score was computed between dataset scores and the predicted scores, to analyze the performance of the designed model. Furthermore, a hybrid deep learning technique was presented by Seth and Agarwal [10], to analyze the DR. The reported technique used digital fundus images to detect and diagnose the diabetic retinopathy. In the training phase, SVM was applied on the EyePACS dataset for experiments and the reported model outperformed the state of the art approaches, in terms of sensitivity and specificity using heterogeneous dataset. The model was quite robust, achieving high precision and recall scores on large heterogeneous data set. ElTanboly et al. [11] developed computer-aided

diagnostic (CAD) framework for the detection of DR using optical coherence tomography (OCT) images. The presented framework contained three stages, Firstly; retina layers were established on the basis of a segmentation approach with the integrated joint model that helps to combine spatial information, shape, and intensity. Secondly, segmented layers measured three features including, thickness, curvature, and reflectivity. Finally, a deep fusion classification network was trained by constraint auto encoder for the classification of normal and diabetic retinopathy and further analyzes the grading of early-stage or mild/moderate diabetic retinopathy. The automatic diagnosis system was introduced by Li et al. [12], for the identification of DR based on DCNN. In the reported work, the authors used fractional max-pooling to derive more discriminative features for classification, instead of the traditional max-pooling approach. A support vector machine (SVM) was applied to classify the discriminative features. In this DR detection model, the Kaggle dataset was used for the training and validation of the fundus images. Additionally, the authors also developed a machine learning-based DR detection application named "Deep Retina" using an ophthalmoscope to obtain the results. Sisodia et al. [13] applied preprocessing and feature selection approaches to identify the DR. The preprocessing approach was implemented on raw retinal data, which was further extracted by resizing, image enhancement, histogram equalization, and green channel techniques. For quantitative analysis, fourteen features were extracted by fundus images. In this technique, the Kaggle dataset was used for the training and validation of the fundus images and classified into three classes including, severe, mild and normal images. The deep CNN based approach was developed by Li et al. [14], to classify the digital retinal fundus photographs. The experiments were performed on two retinal datasets MESSIDOR and DR1 which are publically available. In the defined method, three different approaches were applied including, fine-tuning of network layers, fine-tuning of CNN model and then using CNN models for the features extraction of fundus images. At last, SVM was applied to classify the retinal fundus images. Zhou et al. [15] introduced a deep multiple instance learning (MIL) technique for diabetic retinopathy detection. The presented technique was used for the identification of DR as well as lesions in the retinal fundus photographs. Convolutional neural network was applied for feature extraction and global aggregation was implemented to classify the lesions and DR in fundus images. The experiment was performed on three publically available datasets includes Kaggle, Messidor, and DIARETDB1.

For real-time assistance of diabetic patients, Suriyal *et al.* [16] developed a mobile app for the identification of DR on the basis of deep learning. The designed application was based on tensor flow DNN architecture which trained and validated on fundus images. In the preprocessing phase, the 5×5 filter was used for the quality improvement of fundus images. The presented model was designed with 28 convolutional layers including ResLU and batch norm functions. Gondal et al. [17] presented a supervised learning technique for the localization of DR lesions in fundus images. The developed technique was based on a convolutional neural network to focus on the region of interest for the detection of DR lesions in fundus images. DiaretDB1 dataset was used for experiments and performance evaluation and achieved 95.4% accuracy in DR lesion detection. Gulshan et al. [18] developed a DR detection technique on the basis of deep learning using fundus images. The optimized model was based on a deep convolutional neural network and trained two types of the dataset including EyePACS-1 and Messidor-2 for retinal image analysis. The authorized ophthalmologists analyzed and graded the datasets before experiments. Identification and categorization of retinal lesions are important for the detection of DR. In this context, Paing et al. [19] introduced an approach for the classification of lesions including micro aneurysms, exudates, and blood vessels. The reported approach was based on an artificial neural network to classify the retinal diseases as well as grading and stages using fundus images. M. Purandare and K. Noronha [20] presented a hybrid approach for automatic detection and classification of retinal lesions and diabetic retinopathy using retinal fundus photographs. The reported approach was based on features extraction of bifurcation point, non-segmented texture, exudates area, and blood vessel area. The feature vectors classification was done by the SVM classifier.

The early detection of DR is helpful for patients for recovery and timely treatment. In this context, Prasad et al. [21] introduced segmentation techniques and morphological operations to detect the micro aneurysms, exudates and blood vessels. According to the reported technique, feature extraction was performed by Haarwavlet transformations. PCA was applied for feature selection, one rule and BPNN classifiers were used for fundus image classification as diabetic or non-diabetic. The performance evaluation was reported on the behalf of accuracy, specificity, sensitivity using publically available dataset "DIARETDB1". The retinal lesion detection and classification technique were introduced by Akram, et al. [22] for the grading of diabetic retinopathy. The reported technique based on preprocessing, lesion extraction, and categorization. This method was an extension additional part of the m-Mediods modeling technique plus the GMM classifier to improve the classification accuracy. According to [23], blood vessels were identified through retinal photographs, where the approach based on two types of segmentation methods using standard and modified line operator, were applied to identify the blood vessels. The dual segmentation approaches were applied to achieve a binary vessel map for separate groups of features. Finally, the SVM classifier was used to classify the blood vessels.

In the process of DR lesion detection, Akram, *et al.* [24] introduced the micro aneurysms detection and classification system using filter banks. The presented technique based on three stages; first of all, feature extraction was performed based on candidate regions for micro aneurysms using fundus images. The classification of extracted features

was performed via two well-reputed classifying techniques including GMM and SVM. In this detection technique, an extended modeling approach was introduced naming multimodal mediod to improve the classification accuracy. The automatic diabetic retinopathy detection system was developed by Krishnan and Laude [25] using digital fundus images. Invariant moments, entropies and local binary patterns (LBP), were applied to extract the specified features. Furthermore, a novel approach was introduced namely diabetic retinopathy index (DRI) to integrate index, which was created by various features. In the review article, Faust et al. [26] introduced significant algorithms related to the detection of diabetic retinopathy. The feature extraction was performed by various algorithms using digital retinal fundus images. In the reported survey, several significant classification techniques were also presented. Shahin et al. [27] introduced automatic DR identification and discrimination technique based on the ANN classifier. In the reported technique, homogeneity, entropy, micro aneurysms, exudates, and blood vessels were automatically detected using blurred digital retinal fundus images.

The developed diabetic retinopathy screening system was integrated with vessel density, texture features and global histogram features to find out that the retinal image is ample for DR screening or not [28]. Verma et al. [29] introduced detection and classification techniques, to identify hemorrhages, to identify blood vessels and to classify DR into different classes including NPDR non-proliferative diabetic retinopathy, moderate diabetic retinopathy, and normal retinal. The classification of diabetic retinopathy was classified based on the existence and identification of the hemorrhages and blood vessels. In the reported technique, a color-based segmentation approach was introduced to detect retinal blood vessels using color contrast of blood vessels with its surrounded area. However, density analysis and bounding box approaches were implemented to detect the hemorrhages. At the end, the classification of hemorrhages and retinal blood vessels was performed by a random forest approach. Image analysis approaches were introduced by Singh and Tripathi [30] to early identify the DR. According to the report, different stages and aspects of retinopathy including micro aneurysms, hemorrhages, and exudates were analyzed using digital retinal fundus images. Foveal avascular zone (FAZ) analysis technique was implemented to compute the grading of diabetic retinopathy [31]. The monitoring and grading performance of diabetic retinopathy was measured by analyzing digital fundus photographs. Area of FAZ used to determine the stage of DR through Gaussian Bayes classifier.

From the last few years, the amount of diabetes patients is increased exponentially. In this case, diabetic retinopathy (DR) has become a big challenge, because the people suffering from DR, may lose their eyesight leading towards a complete blindness. Although a lot of researchers have developed various automated methods for the early diagnosis of DR, however at the early stage, many retinal lesions were missed by existing systems and still have room to improve the performance of CAD systems [32], [33]. Previously, none of the existing reviews on the diagnosis of DR covered prestigious techniques, availability of well reputed datasets and research directions comprehensively.

The purpose of this literature review is to demonstrate and investigate the recent development in automated scientific techniques including traditional and deep learning methods to detect diabetic retinopathy based on computer-aided diagnosis systems. Particularly, the analysis of datasets, methods and performance evaluations metrics applied in the existing studies for the detection of diabetic retinopathy. Finally, the analysis of studies is concluded with some suggestions and future directions to make deep learning models more powerful for the detection of diabetic retinopathy.

The major research objectives of this study include:

1. Publically available datasets and their availability in the field of diabetic retinopathy.

2. DR detection methods based on retinal features.

3. Recent state of the art CAD systems for the diagnosis of normal and abnormal retinal features.

4. Performance evaluation metrics that are employed to evaluate DR detection algorithms.

5. Future research directions and challenges, that needs to be addressed by the future researchers working in the area of DR detection.

The remaining part of the article is managed as, Section II presents the research methodologies of diabetic retinopathy detection and segmentation, discussion and observation are covered in section III, future directions and challenges are discussed in section IV, and finally, section V presents the conclusion.

II. RESEARCH METHODOLOGY

In this section, there is an extensive discussion about retinal datasets, diabetic retinopathy detection techniques, and performance evaluation metrics, to learn more about the research development in the area of DR. Generally, in Figure 2, there are basic components of CAD systems.

A. DATASET

Dataset is a collection of records containing useful information, such as insurance or medical records applied by a set of instructions on the system [34]. In this review, all the datasets related to diabetic retinopathy are discussed. The DR datasets contain the records in the form of fundus images. Most researchers employed publically available datasets that can be accessed by the specific links. In the experiments, some of the total images are reserved for the training dataset and some are assigned for testing purposes. For example, Tan, Fujita [35] applied 298 images of CLOEPATRA dataset to classify the diabetic retinopathy, where half of the total images were assigned for training purposes and the remaining half for testing. In the same way, Yang et al. [36] adopted the Kaggle dataset, which is a public dataset contains 22,795 fundus images. The utilization purpose of the Kaggle dataset was to classify the diabetic



FIGURE 2. Basic components of CAD system.

retinopathy. In the experiments, 21995 fundus photographs were used for training and 800 fundus photographs were assigned for testing. Publically available datasets are commonly used for experiments by researchers, which are also known as standard or benchmark datasets including, Messidor, DIARETDB, STARE, DRIVE, Kaggle, E-phtha, and Retinopathy Online Challenge (ROC). The choice and priority of datasets depends on the type of problem and proposed methodologies designed by researchers and experts.

Public and private datasets regarding DR are briefly described one by one in the subsections. TABLE 2 provides the accessible links of datasets for experiments in the field of diabetic retinopathy.

1) PUBLIC DATASETS

• Kaggle

Kaggle dataset is a well known and widely used for the detection of diabetic retinopathy. This dataset contains the total number of 88,702 retinal fundus photographs. Kaggle dataset was produced by EyePACS to facilitate the researchers without any cost. In this dataset, 35,126 fundus photographs were assigned for training purposes and 53,576 for the testing. Gulshan *et al.* [18] used the Kaggle dataset to identify the DR.

• E-Ophtha

E-Ophtha dataset is a publically available dataset and extensively used for the identification of retinal abnormalities and diabetic retinopathy. E-Ophtha dataset for the experiments of diabetic retinopathy was created by a Tele-medical network. E-Ophtha dataset is separated into 2 types as E-Ophtha MA, and E-Ophtha Ex having 381 and 82 retinal photographs, respectively. Kusakunniran *et al.* [37] used E-Ophtha for the detection of hard exudates segmentation.

• Retinopathy Online Challenge (ROC)

ROC dataset is a publically available dataset produced by The University of Iowa to help researchers identify the DR. In this dataset, fundus photographs were captured using the Canon CR5-45 fundus camera. ROC dataset retains the total number of 100 fundus photographs, in which 50 retinal images are assigned for training and the remaining 50 for testing purposes. Chudzik *et al.* [38] applied the ROC dataset for the detection of micro aneurysm.

DIARETDB1

DIARETDB1 is a well-known dataset to identify the DR. DIARETDB1 dataset which retains the total number of 89 retinal fundus images. In this dataset, 5 photographs

48788

 TABLE 2. Accessibility of diabetic retinopathy datasets.

| Serial | Name of datasets | Status | | |
|--------|-------------------------|--------------|---------------|--|
| 110. | | Available | Not-available | |
| 1 | Kaggle | \checkmark | | |
| 2 | <u>E-Ophtha</u> | \checkmark | | |
| 3 | ROC | \checkmark | | |
| 4 | DIARETDB1 | \checkmark | | |
| 5 | DIARETDB0 | \checkmark | | |
| 6 | STARE | \checkmark | | |
| 7 | DRIVE | \checkmark | | |
| 8 | Messidor-2 | \checkmark | | |
| 9 | Messidor | \checkmark | | |
| 10 | CHASE-DB1 | \checkmark | | |
| 11 | FAZ | \checkmark | | |
| 12 | ARIA | \checkmark | | |
| 13 | <u>DR2</u> | \checkmark | | |
| 14 | <u>DR1</u> | \checkmark | | |
| 15 | <u>DRiDB</u> | \checkmark | | |
| 16 | HUPM, Cádiz, Spain | | \checkmark | |
| 17 | KMCM, India | | \checkmark | |
| 18 | LECHC DR India | | \checkmark | |
| 19 | SNDRSP | | \checkmark | |
| 20 | JMU | | \checkmark | |
| 21 | CLEOPATRA | | \checkmark | |
| 22 | Moorfields Eye Hospital | | V | |
| 23 | TMUMDH | | \checkmark | |

were labeled as normal images, while 84 were assigned with diabetic retinopathy. Bui *et al.* [39] applied the DIARETDB1 dataset to find out the cotton wool for the analysis of diabetic retinopathy.

• DIARETDB0

DIARETDB0 dataset is a publically available dataset used in the experiments to detect diabetic retinopathy. In the DIARETDB0 dataset, the total number of fundus images is 130, in which, 110 images were labeled with diabetic retinopathy and 20 were considered normal fundus images. Nijalingappa and Sandeep [40] applied the DIARETDB0 dataset for the identification of diabetic retinopathy using machine learning approaches.

• STARE

STARE dataset is a publically available dataset produced by the University of California, San Diego having the total number of 400 retinal fundus images. All the retinal fundus images of this dataset were taken by the Topcon fundus camera. STARE dataset was applied by Mo and Zhang [41] for the segmentation of retinal vessels using deep learning.

• DRIVE

DRIVE dataset is also a publically available dataset produced by Holland for educational and research purposes. This dataset retains 40 retinal fundus images taken by a non-mydriatic Canon CR5 camera. In this dataset, 20 fundus photographs were assigned for testing and 20 for training. Wang *et al.* [42] applied the DRIVE dataset to identify the retinal blood vessels.

• Messidor-2

The retinal digital fundus images of the Messidor-2 dataset were captured by a non-mydriatic Topcon digital fundus camera with 45 degrees FOV. Messidor-2 dataset holds the total number of 1784 retinal digital fundus images. The messidor-2 dataset is publically available and applied by Abràmoff *et al.* [43] for automatic identification of DR.

• Messidor

Department of ophthalmology, France produced the Messidor dataset, to facilitate the researchers for educational and research purposes. Messidor retains the total number of 1200 retinal fundus photographs. Gegundez-Arias *et al.* [44] applied the Messidor dataset to screen out the DR.

• CHASE-DB1

The Child Health and Study England (CHASE) collected digital fundus images of fourteen children to make a dataset, which is publically available to facilitate the researchers for experimental purposes only. CHASE-DB1 dataset holds 28 retinal digital fundus images of children. Mo and Zhang [41] used CHASE-DB1 dataset for the segmentation of retinal blood vessels.

• FAZ (Foveal Avascular Zone)

FAZ dataset is a public dataset that holds the total number of 60 retinal digital fundus images, in which 35 labeled as diabetic retinopathy photographs along with 25 assigned as retinal normal photographs. Abbas *et al.* [45] applied the FAZ dataset for the detection of "Severe NPDR" using deep visual features.

• ARIA

ARIA dataset holds one hundred and forty-three retinal digital fundus images. The retinal photographs were captured using a Zeiss FF450 fundus camera with fifty degrees of FOV. Arunkumar and Karthigaikumar [46] applied the ARIA dataset for the multi-retinal disease classification using deep learning.

• DR2

DR2 dataset is a publically available dataset that is provided for research experiments. The Federal University of Sao Paulo produced this dataset for the public. DR2 dataset holds the total number of 520 digital fundus photographs taken by non-mydriatic digital camera with 45-degree FOV. Naqvi *et al.* [47] used the DR2 dataset to identify the hard exudates.

• DR1

DR1 dataset was also provided by the Federal University of Sao Paulo to facilitate the researchers in the field of diabetic retinopathy. This dataset holds 234 digital fundus images taken by mydriatic digital camera with 45 degrees of FOV. Li *et al.* [14] applied the DR1 dataset to classify the DR using CNN based transfer learning.

• DRiDB

DRiDB is a publically available dataset that holds fifty retinal digital fundus images. This dataset was provided by the University of Zagreb for educational and research purposes. Prentasic and Loncaric [48] used the DRiDB dataset for the detection of exudates.

2) PRIVATE DATASETS

• HUPM, Cádiz, Spain

This dataset was obtained from the Hospital of Puerta del Mar, Spain. HUPM is a private dataset that was exclusively used by the authors in their research work [45]. The HUPM dataset retains the total number of 250 fundus images, in which 200 photographs were tagged as diabetic retinopathy and 50 photographs were considered normal retinal images.

• KMCM, India

Kasturba Medical College is located in India and is famous about studies of ophthalmology. The dataset obtained by the department of ophthalmology, Kasturba Medical College, was also exclusively used by Ganesan *et al.* [49]. The number of fundus images of this dataset was 340 in total. In which, half of the 170 photographs were labeled as normal retinal images and the remaining 170 images were counted as diabetic retinopathy images. The retinal fundus images were captured by TOPCON, a non-mydriatic digital camera.

• LECHC DR, India

The dataset obtained from Lotus Eye Care Hospital was exclusively used by [50]. In this dataset 122, digital fundus images were recorded. The total number of normal retinal images was 28, while 94 images were considered as diabetic retinopathy images. The digital fundus images were captured by Cannon's non-mydriatic Zeiss digital fundus images.

• SNDRSP

Singapore National DR Screening Program collected 197,085 fundus images in 2013 and 2010. This dataset was exclusively used by [51] for the purpose of research related to diabetic retinopathy and eye diseases.





FIGURE 3. The ratio of DR datasets used in the relevant studies.

• JMU

In this dataset, there are 9939 digital fundus images. The fundus images of the Jichi Medical University dataset were captured by a colored digital camera having forty-five degrees FOV (field of view). Jichi Medical University dataset is a private dataset used by [52].

CLEOPATRA

CLEOPATRA dataset is also a private dataset contains 298 digital fundus photographs. For the detection of diabetic retinopathy, this dataset was collected from fifteen hospitals in the United Kingdom. CLEOPATRA dataset was exclusively used by [35] for automated segmentation of micro aneurysms, exudates, and hemorrhages, using CNN.

• Moorfields Eye Hospital

The Moorfields Eye Hospital, London collected datasets from various ethnicities including Norway, Lithuania, Italy, Saudi Arabia, China, Mongolia, Botswana, and Kenya. This dataset retains 21,536 digital fundus images applied for the detection of diabetic retinopathy. Moorfields Eye Hospital dataset is a private dataset used by [53] to localize the micro aneurysms.

• TMUMDH

Tianjin Medical University Metabolic Diseases Hospital collected fundus images for experiment purposes. The dataset of TMUMDH is a private dataset, which was applied in the research work of [54], to automatically identify the non-proliferative diabetic retinopathy. This dataset contains 414 digital fundus photographs. Figure 3 shows the ratio of the different datasets of DR datasets used in the relevant studies.

B. DR DETECTION AND SEGMENTATION METHODS

Retinal features are very helpful to detect diabetic retinopathy. In the identification of DR, different approaches have been applied to identify the retinal features on the surface of the eye. The comprehensive study related to DR identification and segmentation techniques has been provided in the following subsections. Figure 4 shows the DR detection and segmentation techniques, according to the different retinal features.

1) BLOOD VESSEL SEGMENTATION TECHNIQUES

Detection and segmentation of retinal blood vessels are much important because of helping information for retinal experts to diagnose and identify various retinal diseases including age-related macular degeneration, hypertension, glaucoma, and diabetic retinopathy. Furthermore, retinal blood vessel detection and segmentation are also helpful to diagnose heart and brain stocks, with abnormal changes happen in the vascular system of the retina. The studies related to retinal blood vessel segmentation are more helpful and significance because of non-invasive fundus imaging. Figure 5 demonstrates the pictorial representation of blood vessel extraction and segmentation.

In diabetic retinopathy, contrast improvement and noise removal algorithm were introduced for retinal fundus images



FIGURE 4. DR detection and segmentation methods based on retinal features.



FIGURE 5. Blood vessels extraction and segmentation (a) Changes in vessels (b) original fundus image (c) extracted vasculature [51].

by Sahu et al. [52]. In the reported technique, the author resolved enhancement and de-noising issues using performance parameters including edge preservation index, structural similarity index, peak signal to noise ratio and correlation coefficient. Furthermore, retinal segmentation was performed by Leopold et al. [53], and collected various key performance indicators for the better choice of retinal segmentation. The authors applied the Pixel BNN framework for the high performance of retinal fundus image segmentation. The developed framework was tested on the CHASE_DB1, DRIVE and STARE retinal datasets. The computational speed and performance of the reported technique were analyzed by F1-score.In the medical image processing, Mahapatra et al. [54], designed a multi-stage structure on the basis of the triplet loss function to the stepwise improvement of image quality. Triplet loss function works on the quality output of the previous image, acts as an input for the next image. The application of triplet loss achieves the high definition of images, which help to detect retinal diseases from fundus images. In the blood vessel segmentation, X. Wang, et al. introduced cascade detection and a classification framework for the classification of retinal vessels using complex datasets [55]. The authors applied three types of datasets and achieved 95 to 96% accuracy of vessel segmentation. The defined approach achieved comparatively better performance than other vessel segmentation techniques. According to the authors, the defined method can be utilized for other pattern recognition tasks including image analysis.

Blood vessel segmentation was performed by a fast method with the use of an image matting technique [56]. In the first step, the author applied an automated tri-map to utilize the regional attributes of blood vessels and then implemented the hierarchical image matting technique to get more information about vessel pixels from the region of interest. According to the results, the author improved the performance of vessel segmentation with minimum execution time. In the field of diabetic retinopathy, Hossain and Reza [57] introduced the retinal image segmentation technique on the basis of the Markov random field (MRF). Authors adopted MRF for reported approach and experiments of segmentation, because of better performance than highly complex image segmentation techniques. In the defined article, authors used MRF to make segments of blood vessels through fundus photographs. In the presented technique, Bayesian rule and Markov-Gibbs equivalence were applied to extract the joint distribution and

classification. A deep learning-based blood vessels classifi-

cation technique was introduced by Lahiri et al. [64] using

energy of clique sets respectively. The HRF and DRIVE datasets were used for experiments and performance evaluation. In the image processing, image quality enhancement is also an important task that can help the researchers to get more accurate detection and classification results. Bandara and Giragama [58] introduced an image enhancement technique to make segments of blood vessels through fundus photographs. The image enhancement approach was combined with the Tyler Coye algorithmic approach. The improved approach of the presented model was based on the Hough line transformation for vessel segmentation. The DRIVE and STARE are the public datasets used for the experiments of the developed approach for blood vessel segmentation in the retinal fundus images. The comparative segmentation results and performance evaluation was performed with the five well-known contrast enhancement approaches including, contour-let transform, linear un-sharp masking, local normalization, contrast limited histogram equalization, and wavelet transform.

K. M. Adal, et al. introduced a flexible and robust technique for the detection of red lesions in retinal images [59]. The small red lesions are a major cause of retinal changes and can be detected through small retinal features. For the detection of red lesions, multi-scale blobness technique was applied to measure the effective and simple blobness. Diabetic retinopathy related variations were further identified on the basis of shape features and intensity with the help of the SVM classifier. The retinal fundus image synthesizing problem was addressed using a generative structure by Costa et al. [60]. Specifically, in the defined technique, an adversarial auto encoder was implemented for the synthesis of the retinal vessel network. The generated vessel trees were also applied for the generation of colored fundus photographs. In this technique, both structures achieve the optimal solution of differentiable loss functions. Finally, the resultant structure provides end to end fundus image synthesis model to generate the fundus images according to the requirement of users. The framework for the analysis of retinal images was developed by Maninis et al. [61], provide the segmentation of both retinal vessel and optic disc. The presented model was based on DCNN for deep retinal image understanding. Patwari et al. [62] introduced an algorithmic technique for the calculation and the classification of blood vessels. The specialty of the work was to classify blood vessel parameters including mean diameter, diameter, thickness, length, and area. The vessel segmentation approaches were formulated for retinal vessel extraction. The segmentation was also performed for the identification and detection of boundaries of the blood vessels.

The quality of the image helps for better classification results. In this context, Tennakoon *et al.* [63] presented a novel approach for the classification of the retinal images on the basis of quality. The reported approach was based on computational algorithms using CNN. The results of the experiment demonstrated that both structural and geometrical information was implemented for the image quality retinal photographs. The reported approach was derived from ensemble unsupervised learning. The multiple strategies and de-noised stacked auto-encoder were explored for ensemble members. The presented method used a softmax classifier for the classification of retinal vessels on DRIVE and Kappa datasets. Moreover, Roychowdhury [65] introduced a segmentation approach to segment the blood vessels based on three levels of segmentation. On the very first level, a preprocessing was applied on the green plane of the digital retinal fundus images for feature extraction after high pass filtering moreover; major vessels were extracted using binary images. In the next phase, GMM was used to classify the binary images and feature extraction was performed on the basis of neighborhood pixels. In the third phase, the main regions of the blood vessel were merged based on classified vessel pixels. The experiments were performed using three publically available datasets including, CHASE DB1, STARE, and DRIVE based on the developed algorithm which was partially dependent on training data. Moreover, an improved matched filtering technique was introduced by Odstrcilik et al. [66] to segment the retinal blood vessels through fundus photographs. The reported approach was based on vessel diameters of the high definition retinal fundus images. In this technique, a new high-resolution retinal fundus image database was introduced for better blood vessel segmentation results. Relan et al. [67] introduced the retinal blood vessel classification technique using a Gaussian mixture model with expectation maximization (GMM-EM) classifier based on color features and also applied the quadrant pair wise technique. The developed technique was applied on 35 retinal images having 406 vessels and got accuracy regarding arteries and veins classification as 85% and 87%, respectively. Vessel segmentation, detection, classification is a signifi-

cant task in the medical diagnosis system specifically against diseases including, diabetes, hypertension, and vessel occlusion. In [68], D. Calvo et al. introduced an automatic blood vessel identification approach using fundus photographs. The reported technique derived from morphological operations and filters for vessel detection and classification was done by evaluation of feature points. The classification of micro aneurysm was performed using radon transform without any need for existing information of the retinal morphological attributes and only applied image preprocessing [69]. Retinal vessel detection and classification techniques can help to determine the diameter ratio of veins and arteries [70]. The reported technique was based on the double-ring filter and top-hat transformation to identify retinal blood vessels. The feature extraction was based on vessel segmentation. The classification of target segments into veins and arteries was performed by linear discriminant analysis. The quality assessment technique was introduced based on diagnosis methodologies advised by retinal experts [71]. The classification was performed by the combination of global



FIGURE 6. Micro aneurysms detection (a) Original fundus image (b) MAs identification [81].

clustering with the local texture and sharpness features. Villalobos-Castaldi *et al.* [72] presented an automatic, efficient and fast approach for vessel extraction using retinal fundus images. The reported approach was based on second local entropy to calculate statistic features. In the field of ophthalmology, artificial intelligence and deep learning are performing a vital role to diagnose diabetic retinopathy. In Ting *et al.* [73], explained the contribution of deep learning techniques in the field of ophthalmology to resolve the challenges about diabetic retinopathy detection, glaucoma classification, and vessel segmentation through fundus photographs.

The authors also introduced retinal technical problems, algorithmic results, and deep learning systems for DR and future work in the area of ophthalmology. Moccia et al. [74] presented a review of approximately 100 articles for the motivation of blood vessel segmentation techniques. In the reported review, authors focused on imaging methods, vessel segmentation technique, performance measures, comparative results, advantages and disadvantages of every implemented approach. In the review article, various imaging approaches were discussed including, a deformable model, machine learning, tracking-based, and deep learning techniques. Almotiri et al. [75] introduced retinal vessel segmentation approaches. The view article contains information about different retinal pathologies includes hypertension, glaucoma, and DR. The survey was conducted about retinal fundus images, imaging modalities, preprocessing operations and retinal vessel segmentation techniques. Singh et al. [76] introduced a novel technique with the combination of wave feature extraction, learning algorithms, and different parameter settings. The novelty of the work was the feature extraction of the blood vessel and segmented images for the improvement of performance in terms of accuracy. The designed model was used for the identification of glaucoma through retinal fundus photographs. A cataract classification technique was developed by Harini and Bhanumathi [77]. The experiments were performed on fundus images to classify and grade cataracts. The radial basis function network was applied for the cataract grading into mild and severe. The implementation of the presented method was performed on MATLAB and SVM applied for classification. Estrada *et al.* [78] introduced a graph-theoretic model to classify the veins and arteries using retinal fundus images. The designed model was an extended form of the tree topology estimation model. The extended model composed of domain-specific features, incorporating experts and a global likelihood model. The defined model was analyzed by four retinal databases for the classification of retinal vessels. The methods used in blood vessel segmentation are described in TABLE 3.

2) MICRO-ANEURYSMS DETECTION TECHNIQUES

In fundus images, the micro aneurysms are basic and micro signs of diabetic retinopathy. The leakage of retinal blood vessels is the main cause of micro aneurysms, which later become rounded red spots on the retina. For the identification of DR, the most difficult task is the identification of micro aneurysms because of its tiny size of marks and low contrast between the retinal surface and the red lesion. Figure 6 illustrates the graphical representation of micro aneurysms detection.

The various applications that have been developed to identify the red lesions including micro aneurysms are described in this section. There are a lot of classifiers used to classify the abnormalities in the retina. Chowdhury *et al.* [82] introduced a novel technique using random forest classifier (RFC) to help the ophthalmologists to accurately detect the abnormalities in the retinal images. The author applied a combination of K means clustering technique and machine learning methods, to classify the retinal images. The experiment demonstrates the classification accuracy of retinal diseases with random forest classifiers was 93.58% which is better than the Naïve Bayes classifier having 83.63% accuracy.

TABLE 3. The methods used for blood vessels segmentation.

| Literature | Year | Database | Methods | Performance |
|--------------------------------|------|--------------------------------|---|--|
| Zhun Fan et al. [56] | 2018 | DRIVE, STARE, and CHASE_DB1 | hierarchical image | Accuracy: 96.0%, |
| | | | matting model | 95.7%, and 95.1% |
| Sonali et al. [52] | 2019 | STARE | CLAHE | Improvement in PSNR=7.85%, SSIM=1.19%,CoC=0.12% and EPI=1.28% |
| Henry A. Leopold et al. [53] | 2019 | DRIVE, STARE, and CHASE_DB1 | PixelBNN deep method | Accuracy: 91%, 90%, and 89% |
| Xiaohong Wang et al. [55] | 2019 | DRIVE, STARE, and CHASE_DB1 | Cascade classification framework (Feature extraction, color channel fusion, and dimensionality reduction) | Accuracy: 95.41%, 96.40% and 96.03% |
| Kedir M. Adal et al. [59] | 2017 | Rotterdam Eye Hospital | Multi-scale blobness measured approach | Sensitivity: 98% |
| NafizeIshtiaque | 2017 | DRIVE, HRF | Markov Random Field | Sensitivity: 78.63% |
| Hossain and Sakib Reza [57] | | | | Specificity: 97.67% |
| Bandara and | 2017 | STARE and DRIVE | spatially adaptive contrast | STARE |
| Giragama [58] | | | enhancement technique, Tyler Coye | Accuracy: 94.89% |
| | | | algorithm, Hough line transformation based vessel | TPR: 78.85% |
| | | | reconstruction method | FPR: 3.11% |
| | | | | |
| | | | | DRIVE |
| | | | | Accuracy: 94.11% |
| | | | | TPR: 74.32% |
| | | | | FPR: 3.15% |
| Kevis-Kokitsi | 2016 | DRIVE, STARE, | Convolutional | Accuracy: 98.3% |
| Maninis et al. [61] | | DRIONS-DB, | Neural Networks (CNNs) | |
| | | RIM-ONE | | |
| Manjiri Patwari et | 2016 | diaretdb0, | preprocessing operations, | diaretdb0 Accuracy:95% |
| ai. [62] | | diaretdb1, and | 2D Median Filter | Sensitivity: 95% Specificity:0% |
| | | DRIVE | | diaretdb1 Accuracy 96% |
| | | | | Sensitivity: 96% Specificity:0%, |
| | | | | DRIVE |
| | | | | Accuracy: 98% Sensitivity: 98% |
| | | | | Specificity:0% |
| A.Lahiri et al. [64] | 2016 | DRIVE | Deep Neural Ensemble | Accuracy: 95.33% |
| May PhuPaing et al. | 2016 | DIARECTDB1 | artificial | Accuracy: 96% |
| [19] | | | neural network (ANN) | |
| LiyeGuo et al. [79] | 2015 | Real-world dataset | multiclass discriminant analysis | Accuracy: 90.9% |
| Deepthi K Prasad et | 2015 | DIARETDB1 | morphological operations and | Sensitivity: 97.8% |
| ai. [21] | | | techniques | Specificity: 97.5% |
| | | | techniques | Accuracy: 97.75% |
| Sohini Rovehowdhury et al | 2014 | DRIVE, STARE, and CHASE DB1 | morphological operations and Gaussian Mixture Model | Accuracy: |
| [65] | | | | Drive: 95.2%, STARE: 95.15% and CHASE DB1: 95.3% |
| Ruchir Srivastava et | 2015 | DIARETDB1 | Frangi-based | ROC: 97% |
| ai. [00] | | | Filters | |

C. Lam, et al. developed a deep learning model for the identification of lesions using image patches [83]. In this method, 243 retinal images were tested as a dataset and also verified by two ophthalmologists. The input dataset "Kaggle" was divided into image patches includes micro aneurysms, hemorrhages, exudates, normal-appearing structures, and retinal secularization. The designed convolutional neural network was applied to detect and classify the lesions in five categories. Orlando et al. [84] presented a novel approach for the identification of red lesions on the basis of deep learning and domain knowledge. Features learned by a CNN were incorporated with the handcrafted features for the identification of red lesions. In the classification phase, red lesions were classified by random forest classifier. In the classification of diabetic retinopathy, Cao et al. [85] introduced machinelearning-based micro aneurysms detection techniques. The presented model also included the PCA technique for the identification of micro aneurysms. In this model, 25×25 pixel patches were used as an input to identify micro aneurysms through fundus images. DIARETDB1 was used as a dataset for experiments and performance analysis. A neural network, support vector machine, and random forest were applied used to classify the extracted features and principal component analysis was used for dimensionality reduction.

Automatic red lesion identification technique was presented by Srivastava et al. [80] in diabetic retinopathy including hemorrhages and micro aneurysms using retinal digital photographs. In this approach, Frangi based filtration was performed for blood vessel detection. In the initial stage, preprocessing was done to decompose the input image into smaller sub-images and then filtration was implemented on every sub-image. Extracted features obtained by filters were fed into SVM for further classification of input images whether images contained lesions or not. The experiments were done on 143 fundus images and achieved an accuracy of 87% and 97% for hemorrhages and micro aneurysms, respectively. Hatanaka et al. [86] developed a micro aneurysm detection technique on the basis of feature analysis and double ring filter in digital retinal fundus images. In the reported technique, preprocessing was applied to the retinal dataset and furthermore, the doublering filter was used for the detection of micro aneurysm's regions. Feature extraction of blood vessels was applied by principal component analysis and lesions classification was performed by artificial neural network and rule-based techniques. The identification of DR was performed by Soliman et al. [87] on the basis of ultra-wide field retinal imaging. The UWF utilized ophthalmoscope technology and joined the ellipsoidal mirror to shoot up two hundred degrees of the retina into a single image. To detect the neovascularization and micro aneurysm, Venkatesan et al. [88] presented an approach using digital retinal fundus images. The reported technique was based on color correlogram features extracted by multiple instances of learning approaches and finally classified the diabetic retinopathy. Spatial location, color features, and testing various supervised labeling techniques

The authors introduced retinal micro aneurysms identification and classification method to detect diabetic retinopathy [90]. In the reported technique, authors focused on the reflectivity, visibility, intra retinal location, and draining/feeding vessels found in the retinal fundus image camera, fluoresce in angiography and in optical coherence tomography. Rahimy [91] presented various concepts of deep learning in the field of ophthalmology. In this article, the authors also discussed deep learning applications used in diabetic retinopathy. Moreover, it presented comparative results and performances of deep learning applications and concluded that deep learning techniques can diagnose and detect different diseases that occurred in the field of retinopathy. Finally, in automated fundus images analysis, deep learning techniques achieved outstanding results. Shah et al. [92] introduced the image processing algorithmic technique for the analysis of retinal fundus images. The authors compared the referable diabetic retinopathy (rDR) algorithm and hybrid lesion based algorithm for the classification of the fundus photographs. The presented technique was based on CNN to classify the retinal images and outperformed the hybrid lesion-based algorithms. Mateen et al. [93] introduced deep learning-based methods in image analysis. The presented model helped in the forensic context for the analysis of hyper spectral imaging. The methods used in micro-aneurysms detection are described in TABLE 4.

3) HEMORRHAGES DETECTION TECHNIQUES

In fundus images, the existence of hemorrhages is an early sign and severe cause of diabetic retinopathy. In this case, the accurate and early identification of hemorrhage is much important and helpful for the timely treatment of diabetic patients. The hemorrhages are located in the shallow and deep retina. Bright red and linear-shaped hemorrhages are located in the shallow retina, but dark red and encircled shaped hemorrhages exist into the deep retina. The detection of hemorrhages is applied with various techniques that are discussed in this section. Figure 7 shows the detection of hemorrhages in pictorial format.

In diabetic retinopathy detection, Wu *et al.* [98] introduced a novel approach on the basis of human visual characteristics and two-dimensional Gaussian fitting techniques. The defined approach classifies the hemorrhages on the basis of watershed segmentation and background estimation. First of all, the authors applied the preprocessing method on the fundus images, with the help of an adaptive histogram. In the second step, the feature extraction process was performed for segmentation. In the next step, human visual characteristics and 2D Gaussian fitting techniques were applied for visual features extraction of hemorrhages. Finally, on the basis of visual features, hemorrhages were obtained with an accuracy of 95.42%.

Ayhan and Berens [99] introduced simple and efficient techniques with the use of traditional data augmentation

TABLE 4. The methods used for micro-aneurysms detection.

| Literature | Year | Database | Methods | Performance |
|--|------|--|---|---|
| He Zhao et al. [94] | 2018 | DRIVE, STARE, HRF, IOSTAR | R-sGAN technique | Sensitivity and Specificity: 79.01% and 97.95%, 79.49% and 78.36%, 76.08% and 98.13%, 79.15% and 96.64% |
| Amrita Roy Chowdhury et al. [82] | 2019 | DiaretDB0, DiaretDB1, Tele- ophtha, Messidor | Random Forest classifier | Accuracy: 93.58% |
| Carson Lam et al. [83] | 2018 | E-Ophtha | Standard CNN | AUC: 95% |
| Jos'e Ignacio Orlando et al. | 2018 | DIARETDB1, e- | Handcrafted features, CNN and | AUC: 93.4% |
| [84] | | Ophtha, MESSIDOR | Random Forest Classifier | Sensitivity: 97.2% |
| Arkadiusz Kwasigroch et al. | 2018 | EyePACS | Deep CNN | Accuracy: 82% |
| [9] | | | | Kappa Score: 0.776 |
| Juan Shan and Lin Li [95] | 2016 | DIARETDB | Stacked Sparse Auto-Encoder | F-measure: 91.3% |
| | | | (SSAE) | AUC:96.2% |
| Muhammad Mateen et al. [7] | 2019 | KAGGLE | VGG-19 | Accuracy: 98.34% |
| | | | Architecture with PCA and SVD | |
| Luhui Wu et al. [96] | 2017 | DIARETDB0, DIARETDB1 and Messidor | deep recurrent architecture, | Accuracy: 90% |
| | | | convolution neural network (CNN), long-short- | |
| | | | term-memory (LSTM) | |
| Wen Cao et al. [85] | 2018 | DIARETDB1 | neural | AUC: 98.5% |
| | | | network, support vector machine and random forest | F measure: 92.6% |
| Waleed M. Gondal et al. [17] | 2017 | DiaretDB1 | CNNs | AUC: 95.4% |
| Ruwan Tennakoon et al. [63] | 2016 | D1 | CNNs | Accuracy: 98.27% Sensitivity: 99.12 % |
| | | | | Specificity: 97.46% |
| May PhuPaing et al.[19] | 2016 | DIARECTDB1 | artificial | Accuracy: 96% |
| | | | neural network (ANN) | |
| Manasi Purandare and Kevin Noronha [20] | 2016 | DOKMCM, India | Hybrid System | Accuracy: 92.55%, Specificity: 96%, Sensitivity: 78%, |
| | | | | PPV: 95.12% |
| Deepthi K Prasad et al.[21] | 2015 | DIARETDB1 | morphological operations and | Sensitivity: 97.8% |
| | | | segmentation | Specificity: 97.5% |
| | | | techniques | Accuracy: 97.75% |
| Ruchir Srivastava et al. [80] | 2015 | DIARETDB1 | Frangi-based | ROC: 97% |
| | | | Filters | |
| | | | | |

techniques including color and geometric transformations. The author applied a deep neural network technique to estimate the input predictive uncertainties on the Kaggle dataset to obtain better uncertainty estimates. The fundus image segmentation was introduced on the basis of the R-sGAN approach by Zhao *et al.* [94]. In the reported approach, supervised learning was applied to the synthetic retinal fundus images and obtained better segmentation results after training synthetic retinal dataset. To reduce the computational time of the experiment, Van Grinsven *et al.* [100] introduced an approach to increase the speed of convolutional neural network training for the evaluation of retinal photographs. The identification and classification of retinal hemorrhage were performed on the basis of heuristical samples.



FIGURE 7. Hemorrhages detection (a) original fundus image (b) Hemorrhages identification [97].

Moreover, a splat feature classification technique was performed to detect the hemorrhages in retinal fundus images [101]. In the reported technique, the authors applied a supervised technique to partition the retinal color images into non-overlapping segments. The feature extraction was performed on every splat to define its features related to its neighbors. The authors also applied a filter approach on the basis of the wrapper approach to interacting with neighbor splats.

Large retinal hemorrhage detection and classification technique based on splat features were introduced by Tang et al. [102]. The entire image was covered by the number of splats to classify the retinal hemorrhages based on distinct features. The distinct features include splat with color and spatial location to distinguish blood splats and no blood splats to identify the hemorrhages. Hemorrhages and micro aneurysms detection technique based on morphological operations and pixel classification was introduced by Kande et al. [103]. The experiment was performed using digital retinal fundus images and achieved specificity of 91% and sensitivity of 100%. The fundus image classification technique was introduced by Mateen et al. [7] on the basis of the deep convolutional network. The defined method was based on the Gaussian mixture model, for region segmentation, VGGNet for feature extraction, PCA and SVM for feature selection and softmax for retinal fundus image classification. Kaggle dataset was used for experiments and achieved better results from spatial invariant feature transform and AlexNet. The methods used in hemorrhage detection are described in TABLE 5.

4) EXUDATES DETECTION TECHNIQUES

The existence of exudates on the eye is an early sign of DR. Basically, there are two types of exudates namely; soft exudates and hard exudates. Soft exudates (cotton wool spots) are exemplified as light yellow or white areas with distracted edges but hard exudates are illustrated as yellow waxy patches in the retina. The different ways to detect the soft exudates

and hard exudates have been discussed in this section. Figure 8 illustrates the graphical representation of exudate detection.

Early detection of exudates may help the patients for proper and timely treatment for diabetic retinopathy. In this scenario, Khojasteh *et al.* [106] applied residual networks (ResNet-50) with SVM to get better results for the detection of retinal exudates. The author investigated different convolutional neural networks techniques and then achieved a better technique with the high performance of exudates identification. The obtained results demonstrate that the accuracy of the reported technique was 98%.

analysis In the of diabetic retinopathy, Kaur and Mittal [107] developed exudates segmentation techniques to help the ophthalmologists for early effective planning and treatment. The reported technique used a dynamic decision approach for reliable and accurate segmentation of exudates. The defined model was a robust technique with the selection of threshold values dynamically. The input data of the designed model contains 1307 retinal images having diversity about location, size, color, and shapes. Exudates detection technique was presented by Prentašić and Lončarić [108], using DCNN. Furthermore, deep learning also helped with anatomical landmark detection. The designed framework early detects the exudates from retinal fundus images. Omar et al. [109] developed exudate identification and classification approach through retinal fundus images. The reported approach used a local binary pattern (LBP) and texture features extracted through an artificial neural network. The experiments were performed on public dataset DIARETDB0 having retinal fundus images. The neural network classifier provided accuracy, specificity, and sensitivity as 96.73%, 94.81%, and 98.68%, respectively. Roychowdhury [110] introduced a fundus image classification approach to finding the retinal image features to decrease the complexity of computational time as well as increase the accuracy of DR detection. First of all, feature extraction was performed on the basis of pixels and region of the retinal

TABLE 5. The methods used for hemorrhages detection.

| Literature | Year | Database | Methods | Performance |
|-------------------------------------|------|---|--|---------------------------------------|
| Amrita Roy Chowdhury et al. [82] | 2019 | DiaretDB0, DiaretDB1, Tele- ophtha, Messidor | Random Forest classifier | Accuracy: 93.58% |
| Kemal ADEM et al. | 2019 | Gaziosmanpaşa | adaptive histogram equalization, | Sensitivity: 96.7% |
| [104] | | University | Gabor and Top-hat transformations, iterative thresholding approach | Specificity: 91.4% |
| | | Faculty of Medicine's Department of Ophthalmology | | Accuracy: 94.1% |
| Jun Wu et al. [98] | 2019 | DIARETDB | adaptive histogram equalization, | Sensitivity: 100% |
| | | | background estimation | Specificity: 82% |
| | | | and watershed segmentation, 2D Gaussian fitting | and Accuracy: 95.42% |
| | | | and human visual characteristics | |
| Kedir M. Adal et al. [59] | 2017 | Rotterdam Eye Hospital | multiscale blobness measured approach | Sensitivity: 98% |
| Jos'e Ignacio Orlando | 2018 | DIARETDB1, e- | Handcrafted features, CNN and | AUC: 93.4% |
| et al. [84] | | Ophina, MESSIDOR | Kandom Forest Classifier | Sensitivity: 97.2% |
| Lei Zhou et al. [15] | 2017 | Kaggle, Messidor, | Deep multiple instance learning | Kaggle |
| | | DIARETDB1 | method | ROC: 92.5% |
| | | | | Messidor |
| | | | | ROC: 96.0% |
| | | | | DIARETDB1 |
| | | | | F1 Score: 92.4% |
| | | | | Sensitivity: 99.5% |
| | | | | Precision: 86.3% |
| ShoravSuriyal et al. [16] | 2018 | Kaggle | DCNN | Accuracy: 73.3% |
| Abhay Shah et al. [92] | 2018 | Eyepacs, Messidor-2 | CNNs | Eyepacs |
| | | | | AUC:95% |
| | | | | Messidor-2 |
| | | | | AUC: 98% |
| Waleed M. Gondal et al. [17] | 2017 | DiaretDB1 | CNNs | AUC: 95.4% |
| RuwanTennakoon et | 2016 | D1 | CNNs | Accuracy: 98.27% Sensitivity: 99.12 % |
| ai. [63] | | | | Specificity: 97.46% |
| May PhuPaing et al. | 2016 | DIARECTDB1 | artificial | Accuracy: 96% |
| [19] | | | neural network (ANN) | |
| Mark et al. [100] | 2016 | Kaggle, | convolutional neural network | Kaggle |
| | | Messidor | | AUC: 89.4% |
| | | | | Messidor |
| | | | | AUC: 97.2% |
| LiyeGuo et al. [79] | 2015 | Real-world dataset | multiclass discriminant analysis | Accuracy: 90.9% |
| Deepthi K Prasad et | 2015 | DIARETDB1 | morphological operations and | Sensitivity: 97.8% |
| al. [21] | | | segmentation | Specificity: 97.5% |
| | | | techniques | Accuracy: 97.75% |
| Ruchir Srivastava et | 2015 | DIARETDB1 | Frangi-based | ROC: 97% |
| al. [80] | | | Filters | |



FIGURE 8. Exudate detection (a) Original fundus image (b) Exudate identification [105].

images. In the next step authors performed features ranking technique for optimal classification. Furthermore, the decision forest and decision tree classifier applied to classify the DR lesion and vessels. Automatic exudates detection technique was presented by Prentašić and Lončarić [111] based on DCNN. In the reported technique extraction of exudate, features were performed by CNN plus the SVM classifier was used for classification. Exudates detection on the basis of features segmentation is also a well-known technique [112]. In this approach, the classification into different phases of Non-Proliferative Diabetic Retinopathy (NPDR) was depended on the intensity of pixels and its frequency using digital retinal fundus images. The feature extraction was performed by various techniques including optic disc localization, adaptive threshold using Otsu methodology, image boundary tracing, and preprocessing. Finally, the exudate classification was performed by the Gaussian mixture model.

The grayscale morphological operation was implemented to detect the specific regions and furthermore active contour model was implemented to extract the boundaries of candidates. Finally, the Naïve Bayes classifier was applied to region-wise classify the exudate candidates for detection [113]. Moreover, Mahapatra *et al.* [114] introduced a convolutional neural network-based retinal image quality assessment technique using various handcrafted features. The reported approach was also based on saliency maps to collect the unsupervised information used for the decision making of retinal quality images. The saliency maps collected multiple scales of every pixel to achieve local and global information of retinal images. The methods used in Exudates detection are described in TABLE 6.

5) OPTIC DISC AND OPTIC CUP SEGMENTATION TECHNIQUES

In the fundus images, clinically, optic disc (OD) is considered as a severe fundus element and is an early sign of fovea, macula, optic cup and vessel detection in the digital fundus images. The boundary of optic disc for localization and segmentation specifies the center and a disc contour. In most literature work, geometric and morphological methodologies were used for the extraction of the optic disc. Figure 9 demonstrates the optic disc and optic cup segmentation graphically.

The deep learning-based framework was introduced by Wang et al. [117] to detect optic disc in retinopathy. The author designed CCN based deep learning framework, named as U-net model for the accurate identification of optic disc. In this work, CNN was separately trained on grayscale and color retinal fundus images to obtain the diverse segmentation results from the observed images. The author introduced an overlapped strategy for the identification of local image patches, which was further added to the U-net framework for more segmentation. The S. H. Bhat and P. Kumar introduced the detection of the optic disc and optic cup with the calculation of segmented regions of the optic cup and optic disc [118]. The retinal segmentation technique was introduced by Pekala et al. [119], to segment the optical coherence tomography (OCT) of the retinal images. In this technique, fully convolutional networks on the basis of the Gaussian process works for the segmentation of retinal images. For the performance evaluation of the presented work, a 10-fold cross-validation technique used for the calculation of perpixel unsigned error.

M-Net deep learning model was presented by Fu *et al.* [120], for segmentation of optic disc and optic cup on the same stage. In this method, multi-scale input layers were used including, a side output layer, convolutional network, and multi-label loss functions. The convolutional neural network implemented as the main part of the model to learn about hierarchical representation. Secondly, the side output layer treated as a classifier, and finally, the segmentation map was performed by the multi-label loss function. An automatic technique for early detection of abnormalities in the optic disc was introduced by Alghamdi *et al.* [121]. The designed model was based on supervised learning for the detection

TABLE 6. The methods used for exudates detection.

| Literature | Year | Database | Methods | Performance |
|--|------|--|--|---|
| Parham Khojasteh | 2019 | DIARETDB1 and e- | CNNs | Accuracy: 98% |
| [106] | | Ophtha | ResNet-50 and DRBM | Sensitivity: 99% |
| He Zhao et al.[94] | 2018 | DRIVE, STARE, HRF, IOSTAR | R-sGAN technique | Sensitivity and Specificity: 79.01% and 97.95%, 79.49% and 78.36%, 76.08% and 98.13%, 79.15% and 96.64% |
| Amrita Roy Chowdhury et al. [82] | 2019 | DiaretDB0, DiaretDB1 | Random Forest classifier | Accuracy: 93.58% |
| Sonali et al. [52] | 2019 | STARE | contrast limited adaptive histogram equalization | Improvement in PSNR=7.85%, SSIM=1.19%, CoC=0.12% and EPI=1.28% |
| Carson Lam et al.[83] | 2018 | E-Ophtha | Standard CNN | AUC: 95% |
| Jaskirat Kaur, Deepti | 2018 | STARE, MESSIDOR, | dynamic decision thresholding | Sensitivity: 88.85% |
| Mittal, et al. [107] | | DIARETDB1 and e- Optha EX | | Specificity:96.15% |
| | | 1 | | Accuracy: 93.46% |
| Arkadiusz | 2018 | EyePACS | Deep CNN | Accuracy: 82% |
| Kwasigroch et al. [9] | | | | Kappa Score: 77.6% |
| Waleed M. Gondal et al. [17] | 2017 | DiaretDB1 | CNNs | AUC: 95.4% |
| Pavle Prentašić and Sven Lončarić [108] | 2016 | DRiDB | DNN and landmark detection fusion. | F1 measure: 78% |
| RuwanTennakoon et | 2016 | D1 | CNNs | Accuracy: 98.27% |
| al. [63] | | | | Sensitivity: 99.12 % |
| | | | | Specificity: 97.46% |
| Mohamed Omar et | 2016 | DIARETDB0 | Region-based Multiscale | Sensitivity: 98.68%, |
| al. [109] | | | LBP Texture Approach | Specificity: 94.81 % |
| | | | | Accuracy: 96.73% |
| May PhuPaing et al. | 2016 | DIARECTDB1 | artificial | Accuracy: 96% |
| [19] | | | neural network (ANN) | |
| Sarni Suhaila Rahim et al. [115] | 2016 | DIARETDB0, DIARETDB1, MESSIDOR, DRIVE, STARE and Retinopathy Online Challenge | fuzzy techniques | Accuracy: 93% |
| | | (ROC) | | |
| PavlePrenta [*] si'c and | 2015 | DRiDB | CNNs | F-Score: 77% |
| Lon čari c[111] | | | | Sensitivity: 77% |
| | | | | PPV: 77% |

of abnormalities including, hemorrhages and blood vessels using retinal fundus images.

A novel algorithmic approach was introduced by Roychowdhury *et al.* [122] to classify the optic disc. The defined approach detected location and boundary of vessel origin pixel. In the presented approach, first of all, circular structuring element resized and restructured the fundus images. Secondly, the highlighted regions close to the major blood vessels were obtained by restructured fundus images. In the next phase, the Gaussian mixture model



FIGURE 9. Optic disc and optic cup segmentation (a) original fundus image (b) optic disc segmentation (c) optic cup segmentation [116].

applied for the classification of the bright optic disc and non-optic disc regions. Finally, the classified optic disc region detected as a resultant and required retinal blood vessel. The designed model achieved robust results with a short computational time. The experiment of the reported technique was performed on six publically available retinal datasets including, STARE, MESSIDOR, CHASE DB1, DIARETDB0, DIARETDB1, and DRIVE. Miri et al. [123] introduced a multimodal technique to utilize the related information from spectral domain-OCT volumes and digital fundus images to segment the cup boundaries and optic disc. The multimodal technique was based on machine learning methodologies. Tan et al. [124] introduced the optimal approach to point out the optic cup in digital retinal photographs for the identification of glaucoma. In this technique, the authors made two contributions and worked on the basis of the super pixel categorization approach. Initially, classification issues were addressed with better localization techniques and secondly super pixel resolutions were unified and integrated for significant cup boundary observance. Moreover, Ahmad et al. [125] introduced a glaucoma identification system using retinal fundus images. This reported approach used retinal fundus images for feature extraction, and the extracted features were based on the cup to disc ratio. Glaucoma classification technique was introduced by Noronha et al. [126] to classify glaucoma into three classes including moderate, mild and normal glaucoma. In this approach, linear discriminant analysis was applied for features dimensionality reduction and the extracted features were input to the Naïve Bayesian (NB) and SVM classifiers for glaucoma classification. Yadav et al. [127] presented a classification of glaucoma on the basis of texture features using CNN. The texture features included optic cup which helped for the detection and classification of glaucoma. The neural network was applied as a classifier to classify glaucoma on the basis of extracted texture features using fundus images. Furthermore, Dua et al. [128] presented a glaucoma classification technique using digital fundus images. The feature extraction was performed by biorthogonal, symlets and Daubechies wavelet filters. The reported technique was applied to extract wavelet features using the two-dimensional wavelet transform and obtained retinal energy signatures. Finally, SVM and Naïve Bayes classifiers were applied for the classification of glaucoma.

The automatic glaucomatous classification approach was used by analyzing the optic disk to improve diagnostic efficiency [129]. The reported technique was based on active contour approach with the edge information to segment the cup region. In this technique, eighty digital retinal fundus images were used including fifty-five non-glaucomatous and twenty-five glaucomatous retinal images. Lim *et al.* [130] introduced a technique for the detection and classification of diabetic macular edema using digital fundus images. The feature extraction was performed by the marker-controlled watershed transformation technique. The regions of extracted exudates were used to classify the diabetic macular edema.

Automatic optic disc region segmentation was performed using digital fundus images [131]. The reported approach connected three different methods including fuzzy c-mean (FCM), artificial neural network (ANN), an active contour model (ACM) for optic disc region segmentation. Furthermore, the glaucoma detection technique was performed by Matsuda et al. [132] on the basis of the subspace classifier. The feature extraction technique was based on optimal subspace dimensionality and three image color channels to analyze the f digital fundus photographs. The reported technique achieved better classification results among two existing methods namely the multi-layer perceptrons and learning vector quantization. Moreover, a novel system was introduced to automatically detect glaucoma from color fundus images [133]. The specific preprocessing was performed for glaucoma and then dimension reduction technique was applied to compress the generic feature types. Furthermore, a novel glaucoma risk index (GRI) was extracted by probabilistic classification technique to show the performance of glaucoma detection. In diabetic retinopathy, image processing techniques are commonly used for the detection of glaucoma [134]. In this survey, authors investigated ophthalmic

fundus images and introduced detecting and diagnosing techniques about retinal diseases especially glaucoma.

To enhance the quality of high definition resolution for images is much important for the identification of macula fovea and also for the analysis of fundus images. In Zhang et al. [135], made a contribution in the area of retinopathy to improve the resolution of images. In the reported article, the author introduced the super-resolution technique on the basis of deep learning, to improve the quality of low leveled resolution images. In this technique, three hidden layers were used for feature extraction and to improve the speed of image reconstruction. The experimental results show the high speed of better quality image reconstruction with the use of a super-resolution technique. Li et al. [136] developed a deep learning model to detect the Glaucomatous Optic Neuropathy in the input data. In the defined method, 21 ophthalmologists were hired for the analysis and classification of the fundus images for further steps. In the input dataset, 8000 fundus images were selected for experiments for the evaluation of the defined model. A novel computer-aided diagnosed system was introduced by Raghavendra et al. [137], to detect glaucoma with the use of deep learning techniques. In this technique, the 18 layered CNN model was applied for the training of fundus images to extract robust features. The extracted features were used for the classification of normal and glaucoma classes. In this experiment, 1426 fundus images were used with the ration of 589 normal and 837 glaucoma images.

In the field of image processing, Kermany et al. [138] developed a framework for the analysis of medical images. The defined model was based on transfer learning to train the fractional data. The technique was applied to the OCT images for the classification of diabetic macular edema and age-based macular degeneration. The authors also introduced AI systems for the classification and diagnostic purposes of X-ray images. Perdomo et al. [139] presented an optical coherence tomography (OCT) classification technique on the basis of the convolutional neural network (CNN). The performance of the defined model was calculated by the cross-validation on the given dataset. The obtained result of the presented technique in terms of accuracy was equal to 93.75%. In [140], L. K. Lundberg, et al. discussed optical coherence tomography (OCT) to validate and evaluate the segmentation techniques. For experiments, the authors obtained data from ten normal subjects. The retinal diseases including dry age-related macular degeneration (AMD), wet AMD, vitreomacular traction and diabetic macular edema were investigated.

Wang *et al.* [141] developed an algorithmic approach for the selection of retinal images on the basis of generic quality. The reported approach was helpful for inexperienced individuals from getting consistent interpretable and meaningful data. The defined technique was based on contrast sensitivity function, just noticeable blur, and multi-channel sensation. The support vector machine and decision tree classifier were used for binary classification.

Almazroa et al. [142] introduced, segmentation techniques and methodologies about the cup and disc boundaries. The review paper explained every method, classification techniques and also performance metrics. The glaucoma detection and classification approaches were presented by Gajbhiye and Kamthane [143] using the geometric moment and wavelet features of retinal images. In this technique, three types of wavelet filters including biorthogonal, symlets and daubechies were used for higher-order moments and image decomposition for feature computation. Before the classification phase, the z-score normalization technique was applied to the retinal features. The classification phase was performed with three kinds of classifiers including error back-propagation, k-nearest neighbor and support vector machine. Ibrahim et al. [144] introduced a diabetic maculopathy classification technique using the neuro-fuzzy logic classifier. In the defined method, membership functions were applied to collect a similar group of features of each attribute. The clustering technique partitioned the features having similar attributes into clusters. The equalized universe technique divided the data into equal clusters and the grid partitioning approach partitioned the attributes in equal parts. Finally, the neuro-fuzzy logic system developed corresponding principles for coarsely distributed and finely distributed attributes for effective classification. A deep learning-based glaucoma detection technique was introduced by Issac et al. [145] using digital fundus images. In this technique, blood vessels, neuro-retinal rim, and cup to disc ratio were considered for like features, helped in features extraction for glaucoma detection using learning algorithms. Moreover, Ohno-Matsui et al. [146] introduced a group of myopic macular lesions with the collaboration of clinician-scientists and retinal specialists. The categorization of myopic maculopathy on the basis of fundus images was formulated. Ghosh et al. [147] reported an empirical study to diagnose glaucoma based on grid color moment technique and back propagation neural network (BPNN) classifier for feature extraction and classification. The experiments were performed based on the RIM-ONE database to classify the normal and abnormal retinal images. An automatic glaucoma identification system was developed by Salam et al. [148]. The reported technique was based on the combination of the cup to disc ratio (CDR) and hybrid features. Fundus image classification (suspect, non-glaucoma and glaucoma) was performed on the basis of CDR and classifier. Samanta et al. [149] introduced an approach to apply Haralick features for the classification of glaucoma based on BPNN. The performance of the reported approach was measured by achieved glaucoma classification accuracy (96%).

For the detection of diabetic retinopathy, Venhuizen *et al.* [150] introduced a classification technique to discriminate age-related macular degeneration (AMD) patients from healthy subjects. The reported approach was based on two steps, one of them was unsupervised clustering to extract the image patches and the other belonged to supervised training for the application of image patches, which

TABLE 7. The methods used for optic disc and optic cup segmentation.

| Literature | Year | Database | Methods | Performance |
|-------------------------------------|------|--|---|---|
| Lei Wang et al. [117] | 2019 | ORGIA, MESSIDOR, DRIONS-DB, DIARETDB1, and DIARETDB0 | CNN based U-net model | Overall Accuracy: 96.9% and Sensitivity: 93.9% |
| Preetham Kumar and | 2019 | RIM-ONE | morphological | Accuracy: 98% |
| ShreenidhiBhat [118] | | | operations, Circular Hough | |
| | | | Transform (CHT), Localized Active | |
| | | | Contour Model | |
| Huazhu Fu et al.[120] | 2018 | ORIGA, SCES | DCNN | CDR: 89% |
| | | | | RDAR: 84% |
| M. Pekala et al. [151] | 2019 | U. of Miami | DenseNet fully convolutional networks (FCNs) and Gaussian process | AUC: 98% |
| | | | (GP)-based regression | |
| Hanan S. Alghamdi et | 2016 | DRIVE, STARE, | CNNs | |
| al. [121] | | DIARETOB1 and MESSIDOR, HAPIEE, | | Accuracy: |
| | | KENYA, KFSH and | | DRIVE: 100.0 % |
| | | FAMDI | | DIARETDB1: 98.88 % |
| | | | | MESSIDOR: 99.20 % |
| | | | | STARE: 86.71 % |
| | | | | KENYA: 99.53 % |
| | | | | HAPIEE: 98.36 % |
| | | | | PAMDI: 98.13 % |
| | | | | KFSH: 92.00 % |
| Kevis-KokitsiManinis | 2016 | DRIVE, STARE, | Convolutional | Accuracy: 98.3% |
| et al. [61] | | DRIONS-DB, | Neural Networks (CNNs) | |
| | | RIM-ONE | | |
| SohiniRoychowdhury et al. [122] | 2015 | STARE, MESSIDOR, CHASE DB1, DIARETDB0, DIARETDB1, DRIVE | Morphological Operations, Gaussian Mixture Model | Overall Accuracy: 98.8% |
| Mohammad Saleh Miri et al. [123] | 2015 | Carl Zeiss Meditec, Inc., Dublin, CA | Machine-Learning Graph-Based Approach | Accuracy: 86% |
| Ngan-Meng Tan et al. [124] | 2015 | ORIGA | the existing super pixel classification approach | Accuracy: 85% |

were later used by random forest classifier for classification. The methods used in the optic disc and optic cup segmentation are described in TABLE 7.

C. PERFORMANCE EVALUATION METRICS

The early identification of diabetic retinopathy using digital retinal photographs taken by the fundus camera requires some essential preprocessing techniques before the implementation of image processing algorithms. Numerous preprocessing approaches including median filtering, homomorphism, adaptive histogram equalization, average filtering, and contrast adjustment are used in the standard datasets having fundus images. After the implementation of algorithmic technique on retinal images, mean square error (MSE) and peak signal to noise ratio (PSNR) are determined to evaluate the functionality of an algorithmic approach. The PSNR is a logarithmic decibel value, the higher value of PSNR determines that the processed photograph have better and higher quality against the real photograph.

In the field of healthcare, the data used in medical treatment is commonly divided into two categories; one belongs to the data with disease and others without disease. The correctness level for treatment is estimated by the specificity and sensitivity measures. In the research area of medical science, digital fundus photographs mostly exist in diabetic retinopathy are computed through the specificity and sensitivity of each photograph. The higher values of specificity and sensitivity improve the treatment. The true negative (TN) value shows the non-lesion pixels and true positive value (TP) defines the lesion pixels in the fundus images. On another hand, false negative (FN) shows the lesion pixels which are missed by the algorithmic approach and false positive (FP) indicates the amount of non-lesion pixels that are wrongly traced by the algorithmic approach. The performance evaluation metrics used in the reported studies are described in TABLE 8 to help the researchers in terms of choice, availability of formulas and the significance of evaluation metrics in the literature.

III. DISCUSSION AND OBSERVATION

The digital fundus imaging tool is helpful to screen out the diabetic retinopathy. The diabetic patients mostly need to adopt this examination principle advised by clinical experts to diagnose diabetic retinopathy especially includes mild and moderate retinopathy. In the literature, it is observed that annually 30% of diabetic patients in France and 50% in the United States are advised by clinical experts for DR screening. In this case, the patients need detailed medical checkup assigned by medical doctors. However, automated diagnosis systems for the identification of diabetic retinopathy using fundus images, have been introduced to get fast and authentic classification results. This comprehensive study presents the implication of different computational methodologies including machine learning, image processing, and deep learning to diagnose DR using fundus images. The computerized diagnosis systems are work on the basis of proper segmentation of DR-lesions includes exudates, hemorrhages, and micro aneurysms. The most of studies and methodologies were collected from popular and prestigious databases including PubMed, Elsevier, Mendeley, ACM, and IEEE.

The effectiveness of DR based computer-aided systems depends on the segmentation of features into the fundus images related to diabetic retinopathy, but it is computationally expensive and prone to error. The reliability of the complete system becomes lower by following this step. Moreover, in most of the studies, outdated machine learning and image processing approaches have been used based on large amounts of images, with no quantitative measurements. According to the diagnosis of diabetic retinopathy, there are lots of detection techniques to identify the DR and normal classes which unacceptable in the environment of the real-time DR classification into five classes. In the literature studies, several researchers worked on the assessment of DR classification into five stages and some CAD studies also reliant to monitor changes in retinal characteristics on the basis of domain expert knowledge. A large amount of machine learning approaches have been applied for the grading of diabetic retinopathy but didn't focus on all the aspects of diabetic retinopathy. Furthermore, it is also observed that in the earlier research studies the hardware was not so much competent and advanced to diagnose the diabetic retinopathy with the help of deep learning techniques, but recently, the hardware is also advance and has obtained very good results with the implementation of deep learning to diagnose abnormalities including diabetic retinopathy.

Henceforth, the performance of DR identification assisted by CAD techniques can be developed with the following suggestions:

(a) As an input of CAD systems, large amount of dataset should be collected from various societies with high-resolution images,

(b)Implement fusion of dynamic features, including handengineered and non-hand engineered to achieve better performance of classification particularly in sever DR levels, (c) Utilize some new color appearance/space algorithms for better classification of difficult patterns,

(d) Replacement of 4 levels of diabetic retinopathy database problem with 5 levels,

(e) The monitoring of diabetic macular edema (DME) is also important because it is also a major cause of blindness in diabetic patients.

In the recent studies, retinal experts presented 2 detection parameters namely STARD and DRRI extracted from medical features. It is useful to identify disease levels based on numerical value with various thresholds. Furthermore, it can also be applied to classify the results of DR in terms of quantitative measurements [153].

A. DEEP LEARNING-BASED APPROACHES

Deep learning attained outstanding performances in the area of image processing, particularly in the detection of diabetic retinopathy using fundus images. But, there are some underlying trends and significant challenges of deep learning are still need to discuss. In the applications of computer vision, deep learning opened new directions to solve the complex problems. However, some background knowledge needs to be determined before the implementation of deep learning as the number of convolutional and pooling layers, the number of nodes per layer to achieve the desired output, as well as the choice of model. Deep learning models express the marvelous capability to train a large number of datasets. Typically, it is measured that the small amount of datasets affects and confines the learning and training performance of deep learning. In the literature, there are two types of suggestions that have been introduced to enhance the amount of training data: one of them is related to data collection based on weakly supervised learning approaches and the other is to make the data more generalize on the basis of data augmentation techniques.

B. PERFORMANCE OF TRADITIONAL AND DEEP LEARNING APPROACHES

In the case of diabetic retinopathy detection, a lot of handcrafted and deep learning-based approaches have been introduced, where TABLE 9 demonstrates the accuracies of few cases about lesions (micro-aneurysms, hemorrhages, and exudates) detection to compare the performance of traditional and deep learning approaches. The performance results are



TABLE 8. Performance evaluation metrics used in studies.

| Evaluation Metrics | Formula | Citation in Literature |
|-----------------------------------|---|--|
| Accuracy | $Accuracy = \frac{TN + TP}{TN + TP + FN + FP} \times 100$ | [6, 8, 10-13, 15, 17, 19-21, 55-57, 60, 63-66, 80, 83, 85, 99, 105-107, 109, 110, 115, 116, 119-121, 135, 137, 141, 142, 150, 151][21, 65, 124, 147-149] |
| Sensitivity | Sensitivity = TP / (TP + FN) | [10, 11, 14, 15, 18, 20, 21, 53-55, 57, 59, 62, 63, 82, 84, 94, 98, 104, 106, 107, 109, 111, 117, 134, 136, 137, 139] |
| Specificity | Specificity = TN / (TN + FP) | [10, 11, 14, 18, 20, 21, 53-55, 57, 62, 63, 82, 94, 98, 104, 107, 109, 136, 137, 139, 148] |
| Precision | $\Pr ecision = \frac{TP}{FP + TP}$ | [15, 152] |
| True positive rate (TPR) | TPR = TP / (TP + FN) | [58, 134, 152] |
| Peak Signal to Noise Ratio (PSNR) | $PSNR = 10\log_{10}\frac{(Peakvalue)^2}{MSE}$ | [52, 135] |
| AUC | $AUC = \frac{\sum_{ins_i \in positive class} rank_{ins_i} - \frac{M \times (M+1)}{2}}{M \times N}$ | [14, 17, 60, 83-85, 92, 95, 99, 100, 136, 151] |
| F-Score | $F.Score = \frac{2 \times Recall \times Precision}{Recall + Precision}$ | [15, 53, 55, 61, 82, 94, 95, 108, 111] |
| Structural Similarity Index (SSI) | $SSI(x, y) = [l(x, y)^{\alpha} . c(x, y)^{\beta} . s(x, y)^{\gamma}]$ | [52] |
| Edge Preservation Index (EPI) | $EPI = \frac{(\sum_{m=1}^{M} \sum_{n=1}^{N-1} X'(m, n+1) + X'(m, n))}{(\sum_{p=1}^{M} \sum_{q=1}^{N-1} X(m, n+1) - X(m, n))}$ | [52] |
| Correlation Coefficient (CoC) | $CoC_{x,x'} = \frac{(E[(\mathbf{x} - \rho_x).(\mathbf{x}' - \rho_{x'})])}{\sigma_x \sigma_{x'}}$ | [52] |
| Overlap Score | $OverlapScore = \frac{area(segmentedOD \cap groundtruth)}{area(segmentedOD \cup groundtruth)}$ | [118] |
| G-means | $G-means = \sqrt{SN*SP}$ | [53] |
| Mathews Correlation Coefficient | $P = TP + FP \times N$ $S = TP + FN \times N$ $N = TP + FP + TN + FN$ $mcc = \frac{(TP / N) - S \times P}{\sqrt{P \times S \times (1 - S) \times (1 - P)}}$ | [53, 55] |
| False Positive Rate | FPR = FP / (FP + TN) | [58, 59] |
| Balanced Accuracy (A) | $A = \frac{1}{2}(Sen + Spe)$ | [120] |
| Overlapping Error (E) | $E = 1 - \frac{Area(S \cap G)}{Area(S \cup G)}$ | [120] |
| Positive Predictive Value | PPV = TP / (TP + FP) | [20, 98, 111, 137] |
| Kappa Score | $KappaScore = \frac{Acc - Acc_{prob}}{1 - Acc_{prob}}$ | [9] |

| Technique | Research study | Dataset | Retinal features | Accuracy |
|---------------|----------------------------------|-----------|------------------|----------|
| Deep learning | CNNs [85] | | | 98.50% |
| | | DIARETDB1 | Micro-aneurysms | |
| Traditional | Morphological Operations [21] | | , | 97.75% |
| Deep learning | ANN [19] | | | 96% |
| | | DIARETDB1 | Hemorrhages | |
| Traditional | Random Forest Classifier [82] | | C C | 93.58% |
| Deep learning | CNNs, ResNet-50 [106] | | E 1-4 | 98% |
| Traditional | Fuzzy Techniques [115] | DIAKEIDBI | Exudates | 93% |

TABLE 9. Performance of traditional and deep learning approaches.

based on the same datasets to detect the retinal features using both approaches, where deep learning approaches outperformed the traditional handcrafted approaches.

IV. FUTURE DIRECTIONS AND CHALLENGES

Nowadays, image processing techniques with deep learning have performed a vital role in computer-aided systems to diagnose abnormalities in diabetic retinopathy. There are some possible directions that may help to fully utilize the deep learning approaches in a more effective way. In the literature, it was noted that most research work has been performed with the use of convolutional neural network models to develop deep multi-layer frameworks for the diagnosis of diabetic retinopathy using digital retinal fundus images, but on the other hand, the analysis and explanation of retinal photographs need ophthalmologists, which is time-consuming and very expensive task. Hence, it's necessary to introduce effective deep learning-based approaches that can learn by a limited retinal dataset. The comparison between deep learning techniques to the traditional approaches is explained in the steps.

a) The deep learning-based applications need shared weights for deep networks to set their choices, which could not find in the previous models.

b) Incorporating handcrafted and non-hand crafted features for the achievement of superior generalized models.

c) Establishment of layer-based feature learning approach because each and every layer can learn the following layered features.

d) The generalization feature of the deep learning networks can be improved with the increase of their size to add the number of units and levels in every layer. GoogleNet is an example of this kind of deep learning model having 22 layers.

Additionally, the performance of existing deep learning models can be improved with the combination of dynamic sized DL-based frameworks in the cascade manner. Hence, it can reduce the computational cost as well as the training requirement for individual deep learning models to perform the job independently.

V. CONCLUSION

This study covered a detailed survey about the identification of diabetic retinopathy in the light of almost 150 research articles, summarized with the collection of retinal datasets, adoption of different kinds of methodologies to detect the diabetic retinopathy and select the performance evaluation metrics for the representation of their outcomes. Initially, retinal datasets are discussed and then several kinds of approaches have been explained to detect the retinal abnormalities including retinal neovascularization, hemorrhages, micro aneurysm, and exudates. Moreover, the role of evaluation metrics for computer-aided diagnosis (CAD) systems has been briefly discussed. Finally, the authors' observations have been demonstrated in the discussion to highlight the significance of deep learning based approaches and also provided future directions for scientific researchers against research challenges in the area of diabetic retinopathy.

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