Journal of Positive School Psychology
2022, Vol.6, No.4, 1905-1919
http://journalppw.com

A Systematic Review on Diabetic Retinopathy and Common Eye Diseases Detection through Deep Learning Techniques

N. Durga[1], Dr. D. Kerana Hanirex[2]&Dr. A. Muthukumaravel[3]
[1]Research Scholar, Bharath Institute of Higher Education and Research (BIHER), Chennai.
Email: durga90.n@gmail.com
[2]Associate Professor & Head, Department of Computer Applications, Faculty of Arts & Science, Bharath Institute of Higher Education and Research (BIHER), Chennai.
Email: keranahanirex.cse@bharatuniv.ac.in
[3]Dean-Arts & Science, Professor & Head, Department of MCA,Bharath Institute of Higher Education and Research (BIHER), Chennai. Email: Muthu14673@gmail.com

Abstract

India has approximately 15 million blind people, and the unfortunate reality is that 75 percent of these cases are curable. In India, the doctor-patient ratio is 1:10,000. According to studies, the leading causes of blindness in India are diabetic retinopathy (DR) and glaucoma. Diabetic retinopathy is caused primarily by a person's diabetes and is the leading cause of blindness among working-age people in both developed and developing countries. Glaucoma damages the optic nerve, resulting in blindness. Both diseases are asymptomatic in their early stages, making detection difficult, and if left untreated, they can cause irreversible vision damage. Early detection of diabetic eye disease using an automated system has significant advantages over manual detection as a result of advances in machine learning techniques. A number of advanced studies on diabetic eye disease detection have recently been published. This paper presents a systematic survey of automated approaches to diabetic eye disease detection from a variety of perspectives, including i) available datasets, ii) image pre-processing techniques, iii) deep learning models, and iv) performance evaluation metrics. The survey provides a comprehensive overview of diabetic eye disease detection approaches, including cutting-edge field approaches, with the goal of providing valuable insight into research communities, healthcare professionals, and diabetic patients.

1. Introduction

Diabetic Eye Disease (DED) is a term used to describe a group of eye conditions that include Diabetic Retinopathy, Diabetic Macular Edema, Glaucoma, and Cataract [1]. In patients aged 20 to 74, all types of DED have the potential to cause severe vision loss and blindness. According to the International Diabetes Federation (IDF), approximately 425 million people worldwide were diagnosed with diabetes in 2017. This figure is expected to rise to 692 million by 2045 [2].Eyes are the most used sensory organ of the human body among the five senses. Fig.1 shows the normal anatomical structures of the retina. Fig.2 illustrates a complication of DED in a retina. Serious DED begins with an irregular development of blood vessels, damage of the optic nerve and the formation of hard exudates in the macula region.A significant segment of the mind is utilized in visual processing.Four types of DED threaten eye vision, and they are briefly described in the following subsection:

Diabetic Retinopathy (DR) is caused by damage to blood vessels of the light sensitive tissue (retina) at the back of the eye. The retina is responsible for sensing light and sending a signal to brain. The brain decodes those signals to see the objects around [6]. There are two stages of DR: early DR and advanced DR. In early DR, new blood vessels do not developing (proliferating) and this is generally known as non-proliferative diabetic retinopathy (NPDR). The walls of the blood vessels inside the retina weaken due to NPDR. Narrower bulges (microaneurysms) protrude from the narrower vessel surfaces, often dripping fluid and blood into the eye. Large retinal vessels also start dilating and become irregular in diameter. As more blood vessels become blocked, NPDR progresses from mild to severe.Advanced DR is called proliferative diabetic retinopathy (PDR). In this case, Pressure can build up in the eyeball because the newly grown blood vessels interrupt the normal flow of the fluid. This can damage the optic nerve that carries images from the eye to the brain, leading to glaucoma.

Glaucoma, usually caused by increased pressure inside the eye, is the primary root of visual loss over the globe and cannot be rehabilitated. Detection of glaucoma in its beginning is difficult but can be cured [3]. Glaucoma analysis is based on the medicinal history of the patient's family, intraocular pressure (IOP), retinal nerve fibre layer thickness, and changes in optic disc (OD) structure, for example, the distance across, volume, and region. According to a study, in 2013 overall 64.3 million people in the population aged 40 to 80 years experienced glaucoma. This number can be exceeded to 76 million by 2020 and 111.8 million by 2040 [4]. The effects of diabetes can be observed in different parts of a person's body, including the retina. Symptoms of glaucoma only occur when the disease is slightly advanced; glaucoma is called the silent thief of sight. Therefore, the timely diagnosis of this disease is necessary [5].

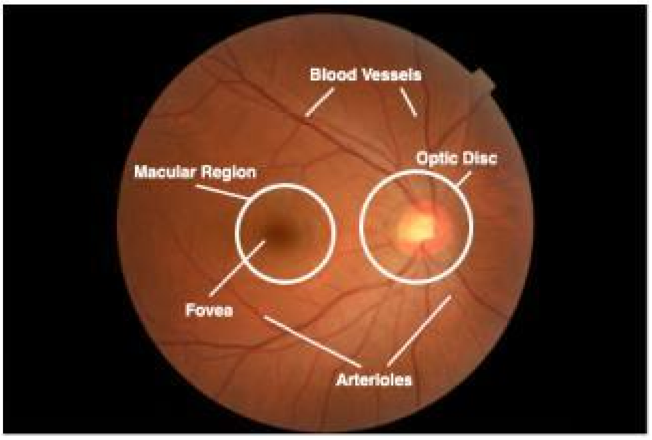

Fig.1. Anatomical structure of the retina

Diabetic macular edema (DME), defined as a retinal thickening involving or approaching the center of the macula, represents the most common cause of vision loss in patients affected by diabetes mellitus. Vascular endothelial growth factor (VEGF) is overexpressed in diabetic eyes and plays a key role in the development of DME. VEGF levels were proven to be elevated in the vitreous and retina in patients with diabetic retinopathy. VEGF causes a breakdown of the blood-retinal barrier by influencing the tight junctions of retinal endothelial cells and leading to accumulation of fluid in the macula. Therefore, intravitreal VEGF inhibitors are ideal candidates to treat DME by counteracting VEGF overexpression.The stages of DME can be categorized into mild, moderate and severe based on the following points [7]:

- Retinal thickening of the fovea at or below 500 μ or 1/3 of its disc diameter.
- Hard exudates, with subsequent retinal thickening, at or within 500 μ of the fovea.
- Retinal thickening at a size that is greater than one disc diameter (1500 μ), and which is within one fovea disc diameter.

A ***cataract*** is a dense, cloudy area that forms in the lens of the eye. A cataract begins when proteins in the eye form clumps that prevent the lens from sending clear images to the retina. The retina works by converting the light that comes through the lens into signals. It sends the signals to the optic nerve, which carries them to the brain. It develops slowly and eventually interferes with our vision. We might end up with cataracts in both eyes, but they usually don't form at the same time. Cataracts are common in older people. Over half of people in the United States have cataracts or have undergone cataract surgery by the time they're 80 years old, according to the National Eye Institute.

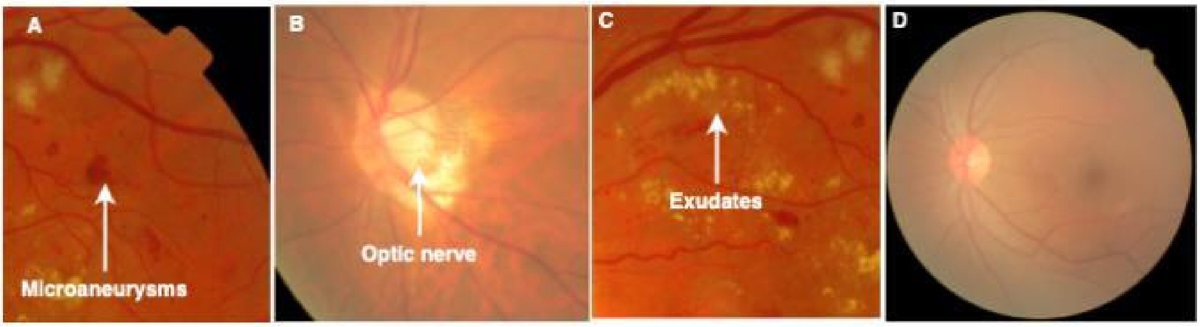

Fig.2. Complications of DED in retina; A. Microaneurysms, narrow bulges (Diabetic Retinopathy), B. Optic nerve damage (Glaucoma), C. Exudates with retinal thickening (Diabetic Macular Edema), D. Degeneration of lens (Cataract)

1.1. Research Problem

Eye screening is a too long and tiresome process because of the keen check-up of each individual patient. Manual detection of DED involves no computer assistance, resulting in longer waiting times between early diagnosis and treatment. Moreover, the initial signs of DED are so minute that even an expert may struggle with its identification. To improve the eye screening procedure, a computer aided diagnosis system (CADx) can be used to give more productive results to the patients to distinguish between healthy and infected retinal fundus images as it is hard for oculists to label this distinction accurately. The continuous expansion of the patient's medical information, such as fundus images, is creating a new challenge in diagnostics, treatment and surveillance. Manual extraction of features from a large volume of fundus images and the discovery of beneficial learning information from these images results in a loss of time between detection and treatment.

1.2. Motivation of the Research Work

Over the last few decades, efforts have been made to develop robust computer-based DED analytics systems using image processing methods and machine learning approaches [8–10]. Though non-DED and DED binary classification using deep learning has achieved strong accuracies in validity. Whereas nonDED and mild-DED (early stage) binary classification as well as multi-stage(mild, moderate and severe) classification from colour fundus images are still an open problem [11,12]. We focus our research primarily on exploring the research gaps in developing an early DED diagnosis (non-DED and mild-DED) classification system based on deep learning, and designing a framework. Throughout our literature review it is noted that none of the preceding studies address the early detection of diabetic eye disease i.e. diabetic retinopathy, glaucoma, diabetic macular edema and cataract in a single system together. Several research studies[13-23] have been identified aimed at classifying stages of an individual diabetic eye disease i.e normal to severe.

1.3. Objectives of the Research Work

In our research study we aimed to develop a single classification system for DED in Children in a particular stage. It is understood that early DED identification with one process is a very important aspect. Seeing the lesions in a specific area or region of eye anatomy can provide specific treatment for the most affected target region of the eye.

1.4. Research Challenges

Deep Neural Network model uses advance mathematical activity to process pixel value in the image where training is performed by integrating the network with diverse examples, as opposed to solid rule-based programming underlying the traditional methodologies. Convolutional Neural Network (CNN) has been thoroughly explored in the DED domain of Deep Learning [13, 15, 16, 18, 24, 25], surpassing previous methodologies namely the recognition of images. Neural networks seek to learn the profound features to identify the sophisticated dimension of mild DED. Regardless, work on detection of DED using deep learning persistently addresses high performance in severe cases, while mild detection of DED remains an open challenge on the other. Our study questions formulated as follows on the way to achieving these aims:

1. How the quality and quantity of the fundus images influence the accuracy of the deep learning techniques.
2. How the transfer learning method can be effective in detecting the mild DED features and improving the accuracy.

3. How to develop the better, deep learning models that will deliver promising DED results.
4. Is there any other eye disease and eye disease dataset be considered for these processes?

1.5. Motivation of the Survey

As mentioned above, DL and TL techniques have their advantages and disadvantages however; several researchers have used these methods to build automatic DED detection systems in recent years. Overall, there is very few review studies published in academic databases which simultaneously address all of the types of DED detection. Thus, this literature review is essential to collate the work in the DED detection field.

Ting et al. [26] published a review article focusing on eye conditions such as diabetic retinopathy, glaucoma, and age-related macular diseases. They selected papers published between 2016 and 2018 and summarised them in their report. They summarized those papers which used fundus and optical coherence tomography images, and TL methods. Their research did not include current (2019-2020) publications that incorporated TL methods into their approach, and they omitted the identification of eye cataract disease from their study scope. Similarly, Hogarty et al. [27] provided a review of current state articles using AI in Ophthalmology, but their focus lacked comprehensive AI methodologies. Mookiah et al. [28], reviewed computer aided DR detection studies, which are largely DR lesion based. Another author, Ishtiaq et al. [29], reviewed comprehensive DR detection methods from 2013 to 2018 but their review lacked studies from 2019 to 2020. Hagiwara et al. [30] reviewed an article for the computer aided diagnosis of Gl using fundus images. They addressed computer aided systems and systems focused on optical disc segmentation. There are a variety of studies using DL and TL methods for Gl detection that have not discussed in their review paper. It is, therefore, important to review papers that consider existing approaches to DED diagnostics. In fact, most scholars in their review article did not address the period of publication years covered by their studies. Current reviews were too narrow, either in terms of disease (DR, Gl, DME and Ca) or in aspects of methodology (DL and ML). Therefore, to address the limitations of the abovementioned studies, this paper offers a thorough analysis of both DL and TL approaches to automated DED detection published between 2014 and 2020 to cover the current DR detection methods built through DL or TL based approaches.

Diabetic eye disease leads to blindness and its prevalence is set to rise continuously. Group of DED damage eye retina at its various parts. Severe DED is the main cause of blindness among adults aged 20-70 years. Glaucoma is the main leading cause in the group of DED which causes irreversible blindness. Diabetic retinopathy (DR) can be classified as non-proliferative DR (NPDR) and proliferative DR (PDR). Specific DR Features can define the different stages. The following are the three subclasses of NPDR as well as PDR. Mild NPDR, Moderate NPDR, Severe NPDR, and PDR [31].Gulshan et al.[32] proposed a DL algorithm for detection of DR. They yielded a result in two validation set of 1748 and 9963 images. The algorithm had the sensitivity of 90.3% and 87.0% and 98.1% and specificity of 98.5% respectively.

Vahadane et al.[33] proposed a system to detected DME in optical coherence tomography scans using deep convolutional neural network (CNN). Their method achieved 96.43% of precision, 89.45% of recall and 0.9281 of F1-score. Prentasic et al. [34] present a fusion based on CNN and landmark detection for detection of exudates. They obtained 0.78 F1 measure. Otalora et al. [35] introduces a CNN model with a label efficient which uses gradient length. Automated segmentation of exudates and other features using ten layers of CNN employed by Tan et al. [36]. Their system used 149 images for training and another 149 images for testing which yielded 0.8758 and 0.7158 of sensitivity for exudates and dark lesions.

Chai et al. [37] in their work the used DL model with retinal images for automatic diagnosis of glaucoma. They used Multi-branch neural network (MB-NN) model to obtain the features. The achieved the 0.9151 of accuracy, 0.9233 of sensitivity and 0.9090 of specificity. Li et al. [38] developed a DL method for detecting non-glaucoma and glaucoma based on visual fields (VFs). Their CNN based algorithm achieved 0.876 of accuracy, 0.826 of specificity and 0.932 sensitivity. Raghavendra et al. [31] proposed an 18 layers CNN framework for glaucoma diagnosis. They evaluated their model with 589 normal and 837 glaucoma images, in which the obtained 98.13% of accuracy, 98% of sensitivity and 98.3% of specificity.

1.6. Contribution

To provide a structured and comprehensive overview of the state of the art in DED detection systems using DL, the proposed paper surveys the literature from the following perspectives:

(1) Datasets available for DED.

(2) Pre-processing techniques applied to fundus images for DED detection.

(3) DL approaches proposed for DED detection.

(4) Performance measures for DED detection algorithm evaluation.

The arrangement of this article is as follows. Section 2 analyses the papers based on the datasets used in their study. Section 3 addresses the image processing techniques used in the prior work. Section 4 analyses the articles based on the classification methods employed. Section 5 discusses the performance metrics employed. Finally, Section 6concludes the paper.

2. Diabetic Eye Disease Datasets

For this study [39], images were acquired from publicly available datasets. Messidor and Kaggle data set were used to acquire DR images. Both the data set contains labelled colour fundus images of DR. Authors such as Franklin et al. [40], Gargeya et al. [41] and Ghosh et al. [42] have used kaggle and messidor dataset. Similarly, colour fundus images of Gl were obtained from (RIGA) retinal fundus images for glaucoma analysis data set[43]. RIGA data set is composed of three different sources (i) Messidor, (ii) Bin Rushed and (iii) Margrabi Eye centre. Al Ghamdi et al. [44] have used RIGA dataset in their study. Finally, fundus images for DME were acquired from Hamilton Eye Institute Macular Edema Data set (HEIMED). Authors in Li et al. [45] used HEI-MED data set in their study. Data set information and their respective link is shown in Table 1. Unfortunately, cataract data set are not publicly available. Authors namely Zhang et al. in [46] mention that they collected cataract data set from Beijing Tongren Eye Center of Beijing Tongren Hospital. These images were graded into four classes; normal, mild, moderate and severe. This data set is not publicly available.

Table 1. Datasets available for automatic Diabetes Eye Detection with source (link)

DED	**Dataset**	**Description**	**Link**	**Other References who used these datasets**
DR	Kaggle	This Data-set consists of 35,126 training images and 53,576 testing images. In total 88,702 images. The images in data set are label with DR stages	https://www.kaggle.com/c/ diabetic-retinopathy-detection/ data	[47]–[52], [53], [54], [55], [56]–[62], [63], [64], [65]
	Messidor	This data-set contain 1200 fundus images in total. These images were obtained by three ophthalmological branch in France. This data set contain labeled DR stages	https://www.adcis.net/ en/Download-Third-Party/ Messidor.html	[52], [66], [67], [68], [69], [65], [70], [71]
Gl.	RIGA	This data-set contains images from three different sources**;** **1)Messidor**: This dataset consist of 460 original images and 460 images were marked manually by six different ophthalmologist. Therefore, total of 3220 marked images. **2)Bin**	https://deepblue.lib. umich.edu/data/concern/ data_sets/3b591905z? locale=en	[72]

		Rushed: This data-set contains 195 original images and 195 images were marked by six different ophthalmologist. Thus in total of 1365 images. **3)Magrabi Eyecenter:** This data-set contains 95 original images and 95 images marked by six different ophthalmologist. These data-set contain 665 images in total		
DME	HEIM	This data-set is obtain from Hamilton Eye Institute Macular Edema Data-set (HEIMED) This data-set contains 169 testing and training images which can be used for the detection of exudates and DME.	https://github.com/lgiancaUTH/HEI-MED	[52]
Ca	Picture Archiving and Communication System (PACS)	In this dataset each fundus image is manually graded by the ophthalmologist as non, mild, moderate, or severe cataract. There are 767 noncataractous, 246 mild, 128 moderate and 98 severe images (total of 1,239).	Publicly unavailable.	[73].

Legend: DED = Diabetic Eye Disease, Gl = Glaucoma, DME = Diabetic Macular Edema, Ca = Cataract

3. Image Preprocessing Techniques in Selected Articles

Images are subjected to numerous image pre-processing steps for visualization enhancement. Once the images are brighter and clearer, a network can extract more salient and unique features. A brief description of the pre-processing techniques used by the researchers addressed in this section. Green channel on the RGB color space provides a better contrast when compared to the other channels. In most of the image pre-processing techniques, green channel extraction is employed. The green channel image produces more information than blue and red channels.

For instance, Li et al. [52] extracted the green channel of the image for exudates detection, where the exudates reveal better contrast from the background. Another popular imagepre-processing technique is contrast enhancement. The application of contrast enhancement further improves the contrast on a green channel image. To improve the contrast of the image, contrast enhancement is employed to the green channel of the image.

For example, again Li et al. [52] have enhanced the contrast on the extracted green channel by employing the Contrast Limited Adaptive Histogram Equalization (CLAHE) method. This enhances the visibility of exudates of a green channel image. Normally, after contrast enhancement, illumination correction is implemented to improve the luminance and brightness of the image. A noise removal filter like Gaussian Filtering is then applied to smooth out the image. The resizing of an image is another popular method of image pre-processing. The image is scaled down to a low resolution image according to the appropriate system.

Li et al. [52] resized their images with various sizes to the same pixel resolution of 512 × 512. Similarly, X. Li [66] resized their image to 224×224 pixel resolution, for all the pre-trained CNN models that used 224×224 size resolution images. The resolution of an image is resized into the resolution required by the network in use. Researchers often have to eradicate and mask the blood vessels and optical discs so that they are not classified as wrong DED lesions. Many DED datasets consist of images with a black border, with researchers generally preferring to segment the meaningless black border to focus on the region of interest (ROI).

For example, Li et al. [52] removed the black border of fundus images using the thresholding method to further focus on the Region of Interest (ROI). Image augmentation is applied when there is an image imbalance (as typically observed in real world settings). Images are mirrored, rotated, resized and cropped to produce cases of the selected images for a class where the number of images is lower than the other large proportion of healthy retina images in comparison with DED retina images. Augmentation is a common strategy for enhancing outcomes and preventing overfitting. It is observed that the distribution of the Kaggle dataset is uneven.

The Kaggle dataset includes 35,126 fundus images annotated as No DR (25810), Mild DR (2443), Moderate DR(5292), Severe DR(873) and Proliferative DR(708). Thus, Li et al. [52], An et al. [74], Nguyen et al. [55], Xu et al. [61], Pires et al. [64], Gargeya et al. [75], Ghosh et al. [58], Van et al. [76], Quellec et al. [50] used the Kaggle dataset and the adopted augmentation technique to balance the dataset. Sometimes the RGB image is transformed into a greyscale image accompanied by further processing. Grayscale conversion is mostly used in approaches where ML is used.

Table 2. Image pre-processing techniques employed in selected studies

GCE	HE	ROI	CLAHE	CE	Re	Au	GSC	BVS	IR	IC	GF	References
✓	✗	✓	✓	✗	✓	✓	✗	✗	✗	✗	✗	Li et al. [52]
					✓							X. Li et al. [66], Al-Bander et al. [77]
✓					✓	✓				✓		Zhang et al. [79]
										✓		Ran et al. [78]
✓	✓			✓	✓							Shaharumet al. [80]
			✓	✓	✓							Gondal et al. [81]
		✓			✓						✓	Mansour et al. [82]
		✓	✓		✓							Yang et al. [62]
	✓			✓		✓						Pires et al. [64]
✓		✓						✓		✓		Orlando et al. [70]
	✓				✓		✓		✓			Dong et al. [83]

4. DNN Classification Models

DNN's classification of normal / severe DED has already shown some promising results but normal / mild are still an open challenge. Bearing in mind the problem of overfitting, one solution could be to increase computational power by increasing the size of the network. Another approach might be object centred recognition such as blood vessels, optic discs, and macular field. Object-oriented detection is more powerful than all image based detection.

4.1. Statement of Significance

Our preliminary work on early detection of DEDs will also have a clear practical significance, as will academic participation.

There have been numerous academic research conducted to diagnose different stages of diabetic retinopathy (normal, NPDR and PDR) using deep learning methods [13, 15, 84]. Similarly, other researchers have identified various stages (normal to severe) of glaucoma using deep learning techniques [17–20]. Deep learning has also been used to diagnose signs of diabetic macular edema and cataracts [21–23]. Our work aims at examining, classifying and detecting all forms of DEDs in children in one method. In addition, we plan to develop a system that will detect the early stage of all types of DED.

4.2. DL Approaches Employing New Network

An alternative to TL is the new network development by the researchers. Out of 65 studies, 21 of them have designed their DL architectures for automated detection of DED. This section presents the list of studies, where the researchers have employed their own built DL models with the classifier indicated, number of layers, model used and results obtained.

Diabetic RetinopathyDoshi et al. [85] detected the severity of diabetic retinopathy using the 29 layers CNN model and detected five stages of DR, and three CNN achieved Accuracy (Acc) of 39.96% on kappa matrix. Gargeya et al. [86] identified diabetic retinopathy using the DL approach. They achieved Accuracy of 94%, specificity of 87% and sensitivity of 93%. Ghosh et al. [58] employed a 28 layers CNN for two and five class classification of diabetic retinopathy. Using Softmax they achieved an Acc of 95% for two class and 85% of Acc for five class classification.Xu et al. [61] employed a 16 layer model for early detection of DR.

Using Softmax classifier they achieved an Acc of 94.50%. Yang et al. [62] employed local and global CNN architectures. Local CNN (10 layers) was used for lesion detection and the global CNN (26 layers) for grading DR. The authors achieved an Acc of 0.9687, specificity of 89.80% and sensitivity of 95.90%. Yu et al. [87] detected exudates using 16 layers CNN. With the Softmax classifier, they achieved an Acc of 91.92%, specificity of 96% and sensitivity of 88.85%. Torre et al. [63] used 17 layered CNN architecture obtaining specificity of 90.8% and sensitivity of 91.1%. Pires et al. [64] proposed 16 layer CNN architecture. They used Messidor-2 and DR2 dataset to test the model. With the neural networks classifier, they achieved Acc of 96.3% in the DR2 dataset and Acc of 98.2% in Messidor-2 and with the Random Forests classifier, they achieved Acc of 96.1% in DR2 dataset and Acc of 97.9% in Messidor-2.

Glaucoma Chen et al. [88] developed six layer CNN model. With the Softmax classifier they achieved an Accof 83.1% and 88.7% in ORIGA [90] and SCES datasets. Raghavendra et al. [89] build an eighteen layer CNN framework to diagnose Gl using 1426 fundus images in where 589 were normal and 937 were with glaucoma. They achieved an Acc of 98.13%, sensitivity of 98% and specificity of 98.3%. Abhishek et al. [91] introduced a novel multi-model DL network named G-EyeNet for glaucoma detection using DRIONS [93] and Drishti-GS [92] datasets. Their experimental findings revealed an Acc of 92.3%.

Diabetic Macular Edema Al-Bander et al. [77] proposed a CNN system to grade the severity of DME using fundus images using the MESSIDOR [94] dataset of 1200images. They obtained an Acc of 88.8%, sensitivity of 74.7% and specificity of 96.5% respectively. Prentavsic et al. [95] introduced a novel supervised CNN based exudate detection method using the DRiDB dataset [96]. The proposed network consists of 10 alternating convolutional and max-pooling layers. They achieved sensitivity of 78%, Positive Predictive Value (PPV) of 78% and FSc of 78% respectively. Tan et al. [98] used the CLEOPATRA [97] image dataset. They obtained sensitivity of 87.58% and specificity of 98.73% respectively.

Cataract Zhang et al. [79] proposed eight layers of DCNN architecture. With the Softmax classifier, they achieved an Acc of 93.52% and 86.69%. Dong et al. [83] used a Softmax classifier with five layer CNN architecture and achieved an Acc of 94.07% and 81.91%, respectively.

4.3. Approaches Employing Combined Dl and Ml

Table 3 shows the studies in which the authors applied a combination of DL and ML classifiers namely: Random Forest (RF), Support Vector Machine(SVM) and Back propagation Neural Network (BPNN) based architectures for DED detection.

Table 3. Studies employing combined DL and ML for automatic DED detection

DED	Models	Layers	Features	References	Classifier	Results
DR	CNN	3	DColor-SIFT, GLOH	[65]	Softmax	AUC = 92.4%, SE = 92.18%, SP = 94.50%
	CNN	10	Shape, Intensity	[70]	RF	AUC = 93.47%, SE = 97.21%
	DBN	3	Shape, Intensity	[99]	SVM	ACC = 96.73%, SE = 79.32%, SP = 97.89%
Gl	CNN	23	-	[77]	RF	ACC = 88.2%, SE = 85%, SP = 90.8%
Ca	DCNN	17	Shallow, residual, pooling	[78]	RF	ACC = 90.69%
	CNN	2	Wavelet, Sketch, Texture	[73]	SVM, BPNN	ACC = 93.2%, 84.5%

Legend: CNN = Convolutional Neural Network, DBN = Deep Belief Network, RF = Random Forests, SVM = Support Vector Machine, BPNN = Backpropagation Neural Network, SE = Sensitivity, SP = Specificity, AUC = Area Under Curve, Acc = Accuracy, DColor-SIFT = Dense Color Scale-Invariant Feature Transform, GLOH = Gradient Location Orientation Histogram.

5. Analysis and Review of Performance Evaluation Metrics

Detailed description of performance measures, namely: specificity, sensitivity, accuracy, area under curve (AUC), precision, f-score, and positive predictive value can be found in [100]. Likewise, Kappa Score, PABAK Index discussions can be found in [101], respectively. In the majority of listed academic papers, the authors used specificity, sensitivity, accuracy and AUC as their assessment metrics to evaluate the efficiency of the classifier. The combined effect of performance metrics found to be used frequently was Sensitivity, Specificity and Accuracy. Instead of Sensitivity, some researchers used Recall. We accommodated Recall under Sensitivity, rather than using it as another success indicator.

6. Conclusion

This review paper provides a comprehensive overview of the state of the art on Diabetic Eye Disease (DED) detection methods. To achieve this goal, a rigorous systematic review of relevant publications was conducted. After the final selection of relevant records, following the inclusion criteria and quality assessment, the studies have been analyzed from the perspectives of 1) Datasets used, 2) Image pre-processing techniques adopted and 3) Classification method employed. The works were categorized into the specific DED types, i.e.DR, Gl, DME and Ca for clarity and comparison. . In this analysis, many publicly available DED datasets have been explored and published. Such as, Kaggle, Messidor, RIGA and HEI-MED dataset were most widely used for the identification of diabetic eye diseases. In this study we addressed the weakness of the publicly available data set and how image pre-processing techniques can be used to fix it. Techniques such as extraction of green channels and enhancement of contrasts using CLAHE have produced better contrast. To prevent over-fitting and neutralize the data disparity, data augmentation was used. To create robust early DED detection system ROI like blood vessels, optic disc and macular region was also been extracted. In deep learning, convolutional neural network architecture is considered to be the most used classification method for the detection of disease using medical images.

References

1. N. E. institute, “Facts about Diabetic Eye Disease,” https://nei.nih.gov/ health/diabetic/retinopathy, 2015, [Online; Last Reviewed: September2015.

2. N. G. Forouhi and N. J. Wareham, “Epidemiology of diabetes,” Medicine, vol. 38, no. 11, pp. 602–606, 2010.
3. Abbas, Q. Glaucoma-Deep: Detection of Glaucoma Eye Disease on Retinal Fundus Images Using Deep Learning. Int. J. Adv. Comput. Sci. Appl. 2017, 8, 41–45. [CrossRef].
4. Tham, Y.-C.; Li, X.; Wong, T.Y.; Quigley, H.A.; Aung, T.; Cheng, C.Y. Global prevalence of glaucoma and projections of glaucoma burden through 2040: A systematic review and meta-analysis. Ophthalmology 2014, 121, 2081–2090
5. Maninis, K.-K.; Pont-Tuset, J.; Arbeláez, P.; Van Gool, L. Deep retinal image understanding. In Proceedings of the International Conference on Medical Image Computing and Computer-Assisted Intervention, Athens, Greece, 17–21 October 2016; Springer: Berlin, Germany, 2016.
6. H. Kolb, “Simple anatomy of the retina by helgakolb,” Webvision: The Organization of the Retina and Visual System, 2011.
7. A. Almazroa, R. Burman, K. Raahemifar, and V. Lakshminarayanan, “Optic disc and optic cup segmentation methodologies for glaucoma image detection: a survey,” Journal of ophthalmology, vol. 2015, 2015.
8. Cheung, C.Y., Tang, F., Ting, D.S.W., Tan, G.S.W. and Wong, T.Y. (2019) Artificial intelligence in diabetic eye disease screening. The Asia-Pacific Journal of Ophthalmology 8(2): 158–164.
9. Vamsi, P. and Chahuan, A. (2020) Machine learning based hybrid model for fault detection in wireless sensors data. EAI Endorsed Transactions on Scalable Information Systems 7(24).
10. Sarker, I.H., Faruque, M.F., Alqahtani, H. and Kalim, A. K-nearest neighbor learning based diabetes mellitus prediction and analysis for ehealthservices.
11. Poplin, R., Varadarajan, A.V., Blumer, K., Liu, Y., McConnell, M.V., Corrado, G.S., Peng, L. et al. (2018) Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning. Nature Biomedical Engineering 2(3): 158.
12. Lam, C., Yi, D., Guo, M. and Lindsey, T. (2018) Automated detection of diabetic retinopathy using deep learning. AMIA Summits on Translational Science Proceedings 2018: 147.
13. Mateen, M., Wen, J., Song, S., Huang, Z. et al. (2019) Fundus image classification using vgg-19 architecture with pca and svd. Symmetry 11(1): 1.
14. Sankar, M., Batri, K. and Parvathi, R. (2016) Earliest diabetic retinopathy classification using deep convolution neural networks. pdf. Int. J. Adv. Eng. Technol 10: M9.
15. Pratt, H., Coenen, F., Broadbent, D.M., Harding, S.P. and Zheng, Y. (2016) Convolutional neural networks for diabetic retinopathy. Procedia Computer Science 90: 200– 205.
16. Wang, Z. and Yang, J. (2018) Diabetic retinopathy detection via deep convolutional networks for discriminative localization and visual explanation. In Workshops at the Thirty-Second AAAI Conference on Artificial Intelligence.
17. Hagiwara, Y., Koh, J.E.W., Tan, J.H., Bhandary, S.V., Laude, A., Ciaccio, E.J., Tong, L. et al. (2018) Computeraided diagnosis of glaucoma using fundus images: A review. Computer methods and programs in biomedicine 165: 1–12.
18. Chen, X., Xu, Y., Wong, D.W.K., Wong, T.Y. and Liu, J. (2015) Glaucoma detection based on deep convolutional neural network. In 2015 37th annual international conference of the IEEE engineering in medicine and biology society (EMBC) (IEEE): 715–718.
19. Orlando, J.I., Prokofyeva, E., del Fresno, M. and Blaschko, M.B. (2017) Convolutional neural network transfer for automated glaucoma identification. In 12th international symposium on medical information processing and analysis (International Society for Optics and Photonics), 10160: 101600U.
20. Al Ghamdi, M., Li, M., Abdel-Mottaleb, M. and Shousha, M.A. (2019) Semi-supervised transfer learning for convolutional neural networks for glaucoma detection. In ICASSP 2019-2019 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP) (IEEE): 3812–3816.
21. Zhang, H., Niu, K., Xiong, Y., Yang, W., He, Z. and Song, H. (2019) Automatic cataract grading methods based on deep

learning. Computer methods and programs in biomedicine 182: 104978.
22. Pratap, T. and Kokil, P. (2019) Computer-aided diagnosis of cataract using deep transfer learning. Biomedical Signal Processing and Control 53: 101533.
23. Zhou, Y., Li, G. and Li, H. (2019) Automatic cataract classification using deep neural network with discrete state transition. IEEE transactions on medical imaging
24. Ahn, J.M., Kim, S., Ahn, K.S., Cho, S.H., Lee, K.B. and Kim, U.S. (2019) Correction: A deep learning model for the detection of both advanced and early glaucoma using fundus photography. PloS one 14(1): e0211579.
25. Sahlsten, J., Jaskari, J., Kivinen, J., Turunen, L., Jaanio, E., Hietala, K. and Kaski, K. (2019) Deep learning fundus image analysis for diabetic retinopathy and macular edema grading. Scientific reports 9(1): 1–11.
26. D. S. W. Ting, L. R. Pasquale, L. Peng, J. P. Campbell, A. Y. Lee, R. Raman, G. S. W. Tan, L. Schmetterer, P. A. Keane, and T. Y. Wong, "Artificial intelligence and deep learning in ophthalmology," British Journal of Ophthalmology, vol. 103, no. 2, pp. 167–175, 2019.
27. D. T. Hogarty, D. A. Mackey, and A. W. Hewitt, "Current state and future prospects of artificial intelligence in ophthalmology: a review," Clinical & experimental ophthalmology, vol. 47, no. 1, pp. 128–139, 2019.
28. M. R. K. Mookiah, U. R. Acharya, C. K. Chua, C. M. Lim, E. Ng, and A. Laude, "Computer-aided diagnosis of diabetic retinopathy: A review," Computers in biology and medicine, vol. 43, no. 12, pp. 2136–2155, 2013.
29. U. Ishtiaq, S. A. Kareem, E. R. M. F. Abdullah, G. Mujtaba, R. Jahangir, and H. Y. Ghafoor, "Diabetic retinopathy detection through artificial intelligent techniques: a review and open issues," Multimedia Tools and Applications, pp. 1–44, 2019.
30. Y. Hagiwara, J. E. W. Koh, J. H. Tan, S. V. Bhandary, A. Laude, E. J. Ciaccio, L. Tong, and U. R. Acharya, "Computer-aided diagnosis of glaucoma using fundus images: A review," Computer methods and programs in biomedicine, 2018.
31. Raghavendra, U., Fujita, H., Bhandary, S.V., Gudigar, A., Tan, J.H. and Acharya, U.R. (2018) Deep convolution neural network for accurate diagnosis of glaucoma using digital fundus images. Information Sciences 441: 41–49.
32. Gulshan, V., Peng, L., Coram, M., Stumpe, M.C., Wu, D., Narayanaswamy, A., Venugopalan, S. et al. (2016) Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs. Jama 316(22): 2402–2410.
33. Vahadane, A., Joshi, A., Madan, K. and Dastidar, T.R. (2018) Detection of diabetic macular edema in optical coherence tomography scans using patch based deep learning. In 2018 IEEE 15th International Symposium on Biomedical Imaging (ISBI 2018) (IEEE): 1427–1430.
34. Prentašić, P. and Lončarić, S. (2016) Detection of exudates in fundus photographs using deep neural networks and anatomical landmark detection fusion. Computer methods and programs in biomedicine 137: 281– 292.
35. Otálora, S., Perdomo, O., González, F. and Müller, H. (2017) Training deep convolutional neural networks with active learning for exudate classification in eye fundus images. In Intravascular Imaging and Computer Assisted Stenting, and Large-Scale Annotation of Biomedical Data and Expert Label Synthesis (Springer), 146–154.
36. Tan, J.H., Fujita, H., Sivaprasad, S., Bhandary, S.V., Rao, A.K., Chua, K.C. and Acharya, U.R. (2017) Automated segmentation of exudates, haemorrhages, microaneurysms using single convolutional neural network. Information sciences 420: 66–76.
37. Chai, Y., Liu, H. and Xu, J. (2018) Glaucoma diagnosis based on both hidden features and domain knowledge through deep learning models. Knowledge-Based Systems 161: 147–156.
38. Li, F., Wang, Z., Qu, G., Qiao, Y. and Zhang, X. (2018) Visual field based automatic diagnosis of glaucoma using deep convolutional neural network. In Computational Pathology and Ophthalmic Medical Image Analysis (Springer), 285–293.

39. RubinaSarki , Khandakar Ahmed and YanchunZhang,"Early Detection of Diabetic Eye Disease through Deep Learning using Fundus Images",EAI Endorsed Transactions on Pervasive Health and Technology,01 2020 - 05 2020, Volume 6 , Issue 22.
40. Group, E.T.D.R.S.R. et al. (1991) Grading diabetic retinopathy from stereoscopic color fundus photographs—an extension of the modified airlie house classification: Etdrs report number 10. Ophthalmology 98(5): 786–806.
41. Franklin, S.W. and Rajan, S.E. (2014) Computerized screening of diabetic retinopathy employing blood vessel segmentation in retinal images. biocybernetics and biomedical engineering 34(2): 117–124.
42. Gargeya, R. and Leng, T. (2017) Automated identification of diabetic retinopathy using deep learning. Ophthalmology 124(7): 962–969.
43. Zhang, J. and Chen, P.H. (2018) Medical imaging 2018: Imaging informatics for healthcare, research, and applications. In Society of Photo-Optical Instrumentation Engineers (SPIE) Conference Series, 10579.
44. Ghosh, R., Ghosh, K. and Maitra, S. (2017) Automatic detection and classification of diabetic retinopathy stages using cnn. In 2017 4th International Conference on Signal Processing and Integrated Networks (SPIN) (IEEE): 550–554.
45. Li, G., Zheng, S. and Li, X. (2017) Exudate detection in fundus images via convolutional neural network. In International Forum on Digital TV and Wireless Multimedia Communications (Springer): 193–202.
46. Zhang, L., Li, J., Han, H., Liu, B., Yang, J., Wang, Q. et al. (2017) Automatic cataract detection and grading using deep convolutional neural network. In 2017 IEEE 14th International Conference on Networking, Sensing and Control (ICNSC) (IEEE): 60–65.
47. W. M. Gondal, J. M. Köhler, R. Grzeszick, G. A. Fink, and M. Hirsch, "Weakly-supervised localization of diabetic retinopathy lesions in retinal fundus images," in 2017 IEEE International Conference on Image Processing (ICIP). IEEE, 2017, pp. 2069–2073.
48. V. Gulshan, L. Peng, M. Coram, M. C. Stumpe, D. Wu, A. Narayanaswamy, S. Venugopalan, K. Widner, T. Madams, J. Cuadros et al., "Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs," Jama, vol. 316, no. 22, pp. 2402–2410, 2016.
49. R. F. Mansour, "Deep-learning-based automatic computer-aided diagnosis system for diabetic retinopathy," Biomedical engineering letters, vol. 8, no. 1, pp. 41–57, 2018.
50. G. Quellec, K. Charrière, Y. Boudi, B. Cochener, and M. Lamard, "Deep image mining for diabetic retinopathy screening," Medical image analysis, vol. 39, pp. 178–193, 2017.
51. P. Roy, R. Tennakoon, K. Cao, S. Sedai, D. Mahapatra, S. Maetschke, and R. Garnavi, "A novel hybrid approach for severity assessment of diabetic retinopathy in colour fundus images," in 2017 IEEE 14th International Symposium on Biomedical Imaging (ISBI 2017). IEEE, 2017, pp. 1078– 1082.
52. G. Li, S. Zheng, and X. Li, "Exudate detection in fundus images via convolutional neural network," in International Forum on Digital TV and Wireless Multimedia Communications. Springer, 2017, pp. 193–202.
53. M. J. van Grinsven, B. van Ginneken, C. B. Hoyng, T. Theelen, and C. I. Sánchez, "Fast convolutional neural network training using selective data sampling: Application to hemorrhage detection in color fundus images," IEEE transactions on medical imaging, vol. 35, no. 5, pp. 1273–1284, 2016.
54. R. Sayres, A. Taly, E. Rahimy, K. Blumer, D. Coz, N. Hammel, J. Krause, A. Narayanaswamy, Z. Rastegar, D. Wu et al., "Using a deep learning algorithm and integrated gradients explanation to assist grading for diabetic retinopathy," Ophthalmology, vol. 126, no. 4, pp. 552–564, 2019
55. Q. H. Nguyen, R. Muthuraman, L. Singh, G. Sen, A. C. Tran, B. P. Nguyen, and M. Chua, "Diabetic retinopathy detection using deep learning," in Proceedings of the 4th International Conference on Machine Learning and Soft Computing, 2020, pp. 103–107.

56. D. Doshi, A. Shenoy, D. Sidhpura, and P. Gharpure, “Diabetic retinopathy detection using deep convolutional neural networks,” in 2016 International Conference on Computing, Analytics and Security Trends (CAST). IEEE, 2016, pp. 261–266.
57. R. Gargeya and T. Leng, “Automated identification of diabetic retinopathy using deep learning,” Ophthalmology, vol. 124, no. 7, pp. 962–969, 2017.
58. R. Ghosh, K. Ghosh, and S. Maitra, “Automatic detection and classification of diabetic retinopathy stages using cnn,” in 2017 4th International Conference on Signal Processing and Integrated Networks (SPIN). IEEE, 2017, pp. 550–554.
59. Y. Jiang, H. Wu, and J. Dong, “Automatic screening of diabetic retinopathy images with convolution neural network based on caffe framework,” in Proceedings of the 1st International Conference on Medical and Health Informatics 2017. ACM, 2017, pp. 90–94.
60. H. Pratt, F. Coenen, D. M. Broadbent, S. P. Harding, and Y. Zheng, “Convolutional neural networks for diabetic retinopathy,” Procedia Computer Science, vol. 90, pp. 200–205, 2016.
61. K. Xu, D. Feng, and H. Mi, “Deep convolutional neural network-based early automated detection of diabetic retinopathy using fundus image,” Molecules, vol. 22, no. 12, p. 2054, 2017.
62. Y. Yang, T. Li, W. Li, H. Wu, W. Fan, and W. Zhang, “Lesion detection and grading of diabetic retinopathy via two-stages deep convolutional neural networks,” in International Conference on Medical Image Computing and Computer-Assisted Intervention. Springer, 2017, pp. 533– 540.
63. J. de La Torre, A. Valls, and D. Puig, “A deep learning interpretable classifier for diabetic retinopathy disease grading,” Neurocomputing, 2019.
64. R. Pires, S. Avila, J. Wainer, E. Valle, M. D. Abramoff, and A. Rocha, “A data-driven approach to referable diabetic retinopathy detection,” Artificial Intelligence in Medicine, 2019
65. Q. Abbas, I. Fondon, A. Sarmiento, S. Jiménez, and P. Alemany, “Automatic recognition of severity level for diagnosis of diabetic retinopathy using deep visual features,” Medical & biological engineering & computing, vol. 55, no. 11, pp. 1959–1974, 2017
66.] X. Li, T. Pang, B. Xiong, W. Liu, P. Liang, and T. Wang, “Convolutional neural networks based transfer learning for diabetic retinopathy fundus image classification,” in 2017 10th International Congress on Image and Signal Processing, BioMedical Engineering and Informatics (CISPBMEI). IEEE, 2017, pp. 1–11
67. M. J. van Grinsven, B. van Ginneken, C. B. Hoyng, T. Theelen, and C. I. Sánchez, “Fast convolutional neural network training using selective data sampling: Application to hemorrhage detection in color fundus images,” IEEE transactions on medical imaging, vol. 35, no. 5, pp. 1273–1284, 2016
68. A. Umapathy, A. Sreenivasan, D. S. Nairy, S. Natarajan, and B. Rao, “Image processing, textural feature extraction and transfer learning based detection of diabetic retinopathy,” in Proceedings of the 2019 9th International Conference on Bioscience, Biochemistry and Bioinformatics. ACM, 2019, pp. 17–21
69. D. J. Hemanth, O. Deperlioglu, and U. Kose, “An enhanced diabetic retinopathy detection and classification approach using deep convolutional neural network,” Neural Computing and Applications, vol. 32, no. 3, pp. 707–721, 2020
70. J. I. Orlando, E. Prokofyeva, M. del Fresno, and M. B. Blaschko, “An ensemble deep learning based approach for red lesion detection in fundus images,” Computer methods and programs in biomedicine, vol. 153, pp. 115–127, 2018.
71. B. Antal and A. Hajdu, “An ensemble-based system for automatic screening of diabetic retinopathy,” Knowledge-based systems, vol. 60, pp. 20– 27, 2014.
72. M. Al Ghamdi, M. Li, M. Abdel-Mottaleb, and M. A. Shousha, “Semisupervised transfer learning for convolutional neural networks for glaucoma detection,” in ICASSP 2019-2019 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP). IEEE, 2019, pp. 3812–3816.
73. J.-J. Yang, J. Li, R. Shen, Y. Zeng, J. He, J. Bi, Y. Li, Q. Zhang, L. Peng, and Q. Wang, “Exploiting ensemble learning for automatic cataract detection and grading,”

Computer methods and programs in biomedicine, vol. 124, pp. 45–57, 2016
74. G. An, K. Omodaka, K. Hashimoto, S. Tsuda, Y. Shiga, N. Takada, T. Kikawa, H. Yokota, M. Akiba, and T. Nakazawa, “Glaucoma diagnosis with machine learning based on optical coherence tomography and color fundus images,” Journal of Healthcare Engineering, vol. 2019, 2019.
75. R. Gargeya and T. Leng, “Automated identification of diabetic retinopathy using deep learning,” Ophthalmology, vol. 124, no. 7, pp. 962–969, 2017
76. M. J. van Grinsven, B. van Ginneken, C. B. Hoyng, T. Theelen, and C. I. Sánchez, “Fast convolutional neural network training using selective data sampling: Application to hemorrhage detection in color fundus images,” IEEE transactions on medical imaging, vol. 35, no. 5, pp. 1273–1284, 2016.
77. B. Al-Bander, W. Al-Nuaimy, M. A. Al-Taee, B. M. Williams, and Y. Zheng, “Diabetic macular edema grading based on deep neural networks,” 2016
78. J. Ran, K. Niu, Z. He, H. Zhang, and H. Song, “Cataract detection and grading based on combination of deep convolutional neural network and random forests,” in 2018 International Conference on Network Infrastructure and Digital Content (IC-NIDC). IEEE, 2018, pp. 155–159
79. L. Zhang, J. Li, H. Han, B. Liu, J. Yang, Q. Wang et al., “Automatic cataract detection and grading using deep convolutional neural network,” in 2017 IEEE 14th International Conference on Networking, Sensing and Control (ICNSC). IEEE, 2017, pp. 60–65
80. S. M. Shaharum, N. H. Hashim, N. A. Talip, M. S. A. Karim, A. A. M. Faudzi et al., “Automatic detection of diabetic retinopathy retinal images using artificial neural network,” in Proceedings of the 10th National Technical Seminar on Underwater System Technology 2018. Springer, 2019, pp. 495–503
81. W. M. Gondal, J. M. Köhler, R. Grzeszick, G. A. Fink, and M. Hirsch, “Weakly-supervised localization of diabetic retinopathy lesions in retinal fundus images,” in 2017 IEEE International Conference on Image Processing (ICIP). IEEE, 2017, pp. 2069–2073.
82. R. F. Mansour, “Deep-learning-based automatic computer-aided diagnosis system for diabetic retinopathy,” Biomedical engineering letters, vol. 8, no. 1, pp. 41–57, 2018
83. Y. Dong, Q. Zhang, Z. Qiao, and J.-J. Yang, “Classification of cataract fundus image based on deep learning,” in 2017 IEEE International Conference on Imaging Systems and Techniques (IST). IEEE, 2017, pp. 1–5
84. Wang, Z. and Yang, J. (2018) Diabetic retinopathy detection via deep convolutional networks for discriminative localization and visual explanation. In Workshops at the Thirty-Second AAAI Conference on Artificial Intelligence
85. D. Doshi, A. Shenoy, D. Sidhpura, and P. Gharpure, “Diabetic retinopathy detection using deep convolutional neural networks,” in 2016 International Conference on Computing, Analytics and Security Trends (CAST). IEEE, 2016, pp. 261–266.
86. R. Gargeya and T. Leng, “Automated identification of diabetic retinopathy using deep learning,” Ophthalmology, vol. 124, no. 7, pp. 962–969, 2017.
87. S. Yu, D. Xiao, and Y. Kanagasingam, “Exudate detection for diabetic retinopathy with convolutional neural networks,” in 2017 39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). IEEE, 2017, pp. 1744–1747
88. X. Chen, Y. Xu, D. W. K. Wong, T. Y. Wong, and J. Liu, “Glaucoma detection based on deep convolutional neural network,” in 2015 37th annual international conference of the IEEE engineering in medicine and biology society (EMBC). IEEE, 2015, pp. 715–718.
89. U. Raghavendra, H. Fujita, S. V. Bhandary, A. Gudigar, J. H. Tan, and U. R. Acharya, “Deep convolution neural network for accurate diagnosis of glaucoma using digital fundus images,” Information Sciences, vol. 441, pp. 41–49, 2018
90. Z. Zhang, F. S. Yin, J. Liu, W. K. Wong, N. M. Tan, B. H. Lee, J. Cheng, and T. Y. Wong, “Origa-light: An online retinal fundus image database for glaucoma analysis and research,” in 2010 Annual International Conference of the IEEE

Engineering in Medicine and Biology. IEEE, 2010, pp. 3065–3068
91. A. Pal, M. R. Moorthy, and A. Shahina, "G-eyenet: A convolutional autoencoding classifier framework for the detection of glaucoma from retinal fundus images," in 2018 25th IEEE International Conference on Image Processing (ICIP). IEEE, 2018, pp. 2775–2779.
92. J. Sivaswamy, S. Krishnadas, G. D. Joshi, M. Jain, and A. U. S. Tabish, "Drishti-gs: Retinal image dataset for optic nerve head (onh) segmentation," in 2014 IEEE 11th international symposium on biomedical imaging (ISBI). IEEE, 2014, pp. 53–56.
93. E. J. Carmona, M. Rincón, J. García-Feijoó, and J. M. Martínez-de-la Casa, "Identification of the optic nerve head with genetic algorithms," Artificial Intelligence in Medicine, vol. 43, no. 3, pp. 243–259, 2008
94. E. Decencière, X. Zhang, G. Cazuguel, B. Lay, B. Cochener, C. Trone, P. Gain, R. Ordonez, P. Massin, A. Erginay et al., "Feedback on a publicly distributed image database: the messidor database," Image Analysis & Stereology, vol. 33, no. 3, pp. 231–234, 2014
95. P. Prentašic and S. Lon ´ cari ˇ c, "Detection of exudates in fundus pho- ´ tographs using deep neural networks and anatomical landmark detection fusion," Computer methods and programs in biomedicine, vol. 137, pp. 281–292, 2016
96. P. Prentašic, S. Lon ´ cari ˇ c, Z. Vatavuk, G. Ben ´ ciˇ c, M. Subaši ´ c, T. Petkovi ´ c,´ L. Dujmovic, M. Malenica-Ravli ´ c, N. Budimlija, and R. Tadi ´ c, "Diabetic ´ retinopathy image database (dridb): a new database for diabetic retinopathy screening programs research," in 2013 8th International Symposium on Image and Signal Processing and Analysis (ISPA). IEEE, 2013, pp. 711–716.
97. S. Sivaprasad, J. C. Vasconcelos, A. T. Prevost, H. Holmes, P. Hykin, S. George, C. Murphy, J. Kelly, G. B. Arden, F. Ahfat et al., "Clinical efficacy and safety of a light mask for prevention of dark adaptation in treating and preventing progression of early diabetic macular oedema at 24 months (cleopatra): a multicentre, phase 3, randomised controlled trial," The Lancet Diabetes & Endocrinology, vol. 6, no. 5, pp. 382–391, 2018
98. J. H. Tan, H. Fujita, S. Sivaprasad, S. V. Bhandary, A. K. Rao, K. C. Chua, and U. R. Acharya, "Automated segmentation of exudates, haemorrhages, microaneurysms using single convolutional neural network," Information sciences, vol. 420, pp. 66–76, 2017
99. R. Arunkumar and P. Karthigaikumar, "Multi-retinal disease classification by reduced deep learning features," Neural Computing and Applications, vol. 28, no. 2, pp. 329–334, 201
100. M. Sokolova and G. Lapalme, "A systematic analysis of performance measures for classification tasks," Information processing & management, vol. 45, no. 4, pp. 427–437, 2009.
101. G. Chen, P. Faris, B. Hemmelgarn, R. L. Walker, and H. Quan, "Measuring agreement of administrative data with chart data using prevalence unadjusted and adjusted kappa," BMC medical research methodology, vol. 9, no. 1, p. 5, 2009