Recent Innovations in Automated Detection and Classification of Diabetic Retinopathy

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Abstract—Due to the increasing prevalence of diabetic retinopathy worldwide, it's an urgent need to develop smart system that help to detect disease using one of the modern technologies. Artificial intelligence is one of the popular techniques nowadays which has the ability to learn from experience and carry out human-like tasks. Large number of researches have been conducted to find out effective medical diagnosis methods for numerous diseases. Likewise, huge number of researches have been done that discuss automated detection and classification of diabetic retinopathy. This paper reviews the existing methodologies, datasets, sensitivity, specificity and classification accuracy in diabetic retinopathy.

Keywords— Diabetes Mellitus; Diabetic Retinopathy; NPDR; PDR; Artificial intelligence; Machine Learning; Image Preprocessing; Deep Learning; CNN; RNN; RBM; Autoencoders; Kaggle; Messidor-2; DRIVE; TensorFlow; Keras; Theano; Sensitivity; Specificity; Accuracy

I. INTRODUCTION

Diabetes mellitus is one of the most challenging challenges in the world for the 21st century and it's a chronic and complex disease that affects a large number of people. Diabetes is a chronic disorder that causes the body to be unable to use energy from its food sources because of lack of the insulin hormone that is responsible for enhancing the ability of cells to absorb glucose to produce energy. Symptoms of diabetes begin to appear and develop gradually in diabetes patients such as frequent urination, weight loss, nausea and vomiting, excessive thirst and appetite, and slow healing wounds.

Over time, diabetes mellitus can affect the body's main organs and leads to heart disease, stroke, amputation, kidney failure, blindness and early death. Diabetic retinopathy is one of diabetes complication that affects the eye and occurs as a result of damage to the blood vessels of light-sensitive tissues in the back of retina. The hyperglycemia continuous causes to a blockage in the tiny blood vessels that nourish the retina. Thus, the eye tries to create new blood vessels, but these vessels do not grow properly and can bleeding easily. Diabetic retinopathy in its early stages does not cause any changes in vision, but with the development of the disease, the level of vision worsens significantly may lead to blindness.

Diabetic Retinopathy is one of the main causes of poor vision and blindness. The exact distinction between the different grades of diabetic retinopathy to define each grade's features make the recognition task to classify DR very challenging. It has been shown that periodic screening of DR and timely treatment reduces the risk of blindness [4]. Automated detection of diabetic retinopathy is essential to address these challenges as well as to detect the disease at early stage to prevent blindness with appropriate treatment using advances technical medical developments [3].

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II. DIABETES MELLITUS

Based on the high proportions of patients with diabetes, diabetes mellitus (DM) is a real health hazard in all countries, including Oman. DM is a disease in which the blood sugar rises above the normal rate due to a total or partial deficiency in the production of insulin hormone from pancreatic cells or weakness in the effectiveness of insulin at the level of cells and tissues. DM can be categorized into three types which are: Type1 diabetes (T1D), Type2 diabetes (T2D) and Gestational diabetes mellitus (GDM). T1D is also called insulin-dependent diabetes. It occurs when the total lack of Insulin hormone production of pancreatic cells. T1D can occur at any age, but usually diagnosed in children and young people. This type is the least common type of diabetes, affecting only 10-15% of all diabetics. Whereas, T2D is a partial decrease in the production of insulin hormone with weakness in its activity at the level of cells and tissues. It also called insulin-dependent diabetes, or diabetes, which appears in adulthood. This type of diabetes is the most common type, affects 85-90% of all diabetics. The third type of diabetes is GDM which occurs during pregnancy and usually goes after the baby's birthday. Diabetes mellitus often leads to many serious complications which affect the patient's health and life and reduces the average age of the patient. Potential complications of DM include heart attack, stroke, kidney failure, amputation, blindness and nerve damage. Poor diabetes control during pregnancy increases the risk of fetal death and possibility appearance of other complications [49]. The map in figure1 shows the information and projections on diabetes worldwide [50].

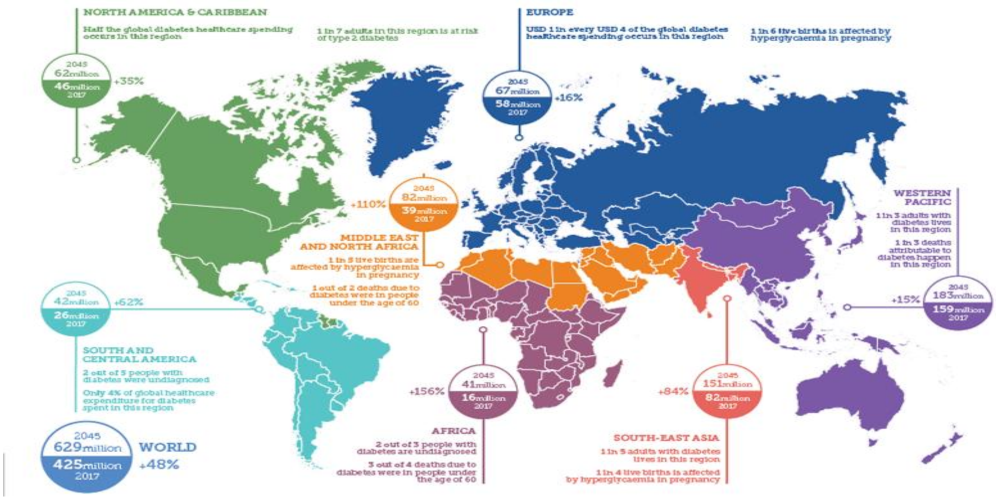

Figure 1: Information & and projections on diabetes worldwide [50].

III. DIABETES COMPLICATIONS (DIABETIC RETINOPATHY)

Diabetes leads to multiple complications that are associated with two main factors: the rate blood glucose and years of disease. One of the serious complications of diabetes is diabetic retinopathy (DR). DR is one of the diabetes complications that affects the eye and occurs as a result of damage to the blood vessels of the light-sensitive tissues in the back of the eye (retina). At early stage, the symptoms of DR don't appear or just cause minor vision problems but can eventually lead to blindness. However, with the progression of the disease, the symptoms can appear and include the following: spots or dark lines appear during vision, Foggy vision, Vibrate vision, Weak vision of colors, Dark or empty areas of vision and Loss of vision [48].
Diabetic retinopathy can be categorized into two main types which are non-proliferative retinopathy (NPDR)and proliferative retinopathy (PDR). The most common type is NPDR and is caused by fluid leakage to the retina or clogged blood vessels, whereas the second type is caused by the abnormal growth of new blood vessels and bleeding or rupture [51]. Diabetic retinopathy usually develops from non-proliferative to proliferative disease. This development takes a few years.

IV. DIABETES MELLITUS IN OMAN

One of the most common diseases in Oman today is diabetes and the rate of infection among the Omani population is 10%. That means of every 100 people, 10 people are infected with this disease. It is a chronic disease that needs to be treated or, in other words the life of the patient in risk if not follow regular treatment [47].
A study conducted by a team of researchers in the medical field in the Sultanate of Oman and published by the medical journal of the University of Sultan Qaboos that there is widespread prevalence of diabetes in the Omani society. The study pointed out that it is expected to double cases in the coming years, which indicates the existence of a health problem must be avoided. The study aimed to assess the prevalence of diabetes in the Sultanate during the past years. The study team analyzed three international surveys, including Oman, to study the prevalence of diabetes, which was conducted between 1991 and 2010. The study aimed to analyze data for the age group of 20 years and above to study the prevalence of type I and type II. The first type occurs always the human at an early age due to a defect in the pancreas so that not excreted enough insulin, whereas the second type is the most common form of human at a young age and occurs due to poor lifestyle. The study found that the prevalence of the second type of disease in females is higher than that of males. In contrast, the proportion of unrecognized cases in males is higher than that of females. The results of this study indicate that it is expected that by 2050 more than 350,000 people in the Sultanate will have diabetes Type II, an increase of 174% from the currently projected in 2015. The study stressed that this increase is very frightening and should put diabetes at the forefront of diseases to avoid, by spreading awareness in the community and encourage eating healthy and exercise, knowing that 80% of the cases can be avoided only by modifying the lifestyle to be healthy and vital. The study is part of a number of studies that indicate the prevalence of a number of chronic diseases in Omani society, mostly due to changing lifestyle, unhealthy food and lack of exercise [46].
The increase in the prevalence of diabetes and the increase in life-expectancy for people with DM will significantly increase visual disability due to complications of diabetes in the eye. Based on World Health Organization (WHO) statistics [1], the range of diabetic retinopathy prevalence reported for Oman is between 14.5% and 42.2%. Means that, there are between 16,000 and 47,000 cases of diabetic retinopathy throughout the country. According to the American Academy of Ophthalmology [56], 93 million people with diabetic retinopathy, that means 1 out of 3 persons with diabetes are affected by diabetic retinopathy. The GCC citizens had the highest

comparative prevalence of diabetic retinopathy in the world as shown in table 1.

Table 1: Prevalence of Diabetic Retinopathy in GCC citizens

GCC citizens	Prevalence Rate
Saudi Arabia	19.7%
Qatar	23.5%
Kuwait	up to 40%
UAE	19%
Bahrain	25.8%

V. ARTIFICIAL INTELLIGENCE

Artificial intelligence (AI) is one of modern technique that would act as a useful and auxiliary technical for diabetic retinopathy screening and providing diagnostic support but cannot replace the role of physicians in clinical diagnosis [4]. AI is a term proposed by John McCarthy in 1956 which refers to software or hardware that shows intelligent behavior [8]. Deep integration between AI and ophthalmology has the prospective to revolutionize pattern of disease diagnose and create a significant clinical effect [7]. With the future development of artificial intelligence will generate new medical developments and the ophthalmologists will need to learn how to take advantage of these technical developments to improve medical care.

Numerous artificial intelligence research studies have been performed to multiple diseases such as skin cancer classification, breast histopathology analysis, lung cancer detection, cardiovascular diseases' risk prediction, etc. [7]. These inspiring studies encourage various studies to also performed AI algorithms in ophthalmology. Artificial intelligence algorithms together with various accessible datasets, such as Kaggle, Messidor, and EyePACS, would achieve great achievements on multiple ophthalmological issues [9]. Li et al. [26] conclude in their study that AI-based DLA can be used with high accuracy to detect DR in retinal images. They state also that artificial intelligence technology has an ability to increase the efficiency of screening diabetic retinopathy.

VI. MACHINE LEARNING

Machine learning (ML) is a subset of artificial intelligence that occurred in 1980s and supports the modern society in many ways [41]. ML is a method that detect patterns automatically in data and then integrate this information to predict the future data [7]. This modern technology is used in many applications and became a prevalent technology in various products for example smart phones, cameras, smart machines. Furthermore, it is beneficial for many areas such as speech recognition, object recognition, edge detection and etc.

ML in this age, indicates the promise of producing accurate and consistent estimates. ML system efficiently learns how to predict from training dataset [36]. This technique has two types of methods: deductive and inductive. Deductive learning methods works on current knowledge and facts and assumes new knowledge from the old. Whereas inductive methods generate systems by extracting patterns and rules out of massive datasets [36].

ML can be categorized into two methods: supervised machine learning and unsupervised machine learning. The supervised machine learning method learns to accomplish aims based on “Ground Truth”. The training dataset come with "labels" to be used by the ML algorithm to distinguish the data. While, the unsupervised machine learning method doesn't need to label training datasets beforehand [37].

VII. IMAGE PREPROCESSING

Processing of retinal image is used extensively to detect eye diseases in an effective and easy way as well as assists ophthalmologists to screen their patients in more efficient manner [20]. Preprocessing of the images is very important to get the accurate features for improving the accuracy of the later stages. Dutta et al. [16] state that lacking image pre-processing stages and noisy images might leads to lower accuracy. This study was considered on image preprocessing through different filter mechanisms that improves the image features. The basic steps involved in the image pre-processing is re-sizing the images. Before input the images into the model for classification, the images should convert into gray-scale [17].

Li et al., [37] proposed in their research work three steps in preprocessing. The initial step is rescaling the input images to the 540 pixels. After rescaling input images, the value of local average color is subtracted and mapped to 50% grayscale to eliminate the color divergence produced by different ophthalmoscope. The final step is eliminating the margin by cutting 10% from the border of the fundus images. Chandrakumar et al [17] used image editor tool for color balance adjustment, rotate, contrast adjustment or cropping. At image preprocessing stage, they used NumPy package to resize image and convert into monochrome. Chandore et al [18] used Python Imaging Library tool for contrast adjustment, color balance adjustment, crop or rotate images. They used NumPy package for black borders and resize image at preprocessing stage. Sayed et al [19] converted the RGB retinal image into grey-scale image. The proposed system made use of the Grayscale conversion, Adaptive Histogram Equalization, Discrete Wavelet Transform, Matched filter and Fuzzy C-means segmentation for preprocessing the retinal photographs of poor quality.

VIII. DEEP LEARNING

Deep learning (DL) is a bourgeoning technology of machine learning that occurred in 2000s and has revolutionized the AI world. DL method is a leading technology with many potential applications in ophthalmology [6]. The very significant property of DL techniques is that it can learn feature representations automatically therefore avoiding time-consuming. The considerable advances in the ML algorithms, and reasonable cost of computing hardware are mainly critical reasons for the deep learning booming [41].

DL uses learning methods of representation at multiple levels of abstraction to process input data without the need to engineer manual feature for automatic recognition of intricate structures in high- dimensional data. DL has achieved significantly higher accuracies than conventional techniques in many domains, such as voice recognition, natural language processing, and computer vision [7].

In recent years, deep learning method has achieved a major success as a new machine learning technique and algorithms have been widely used in the field of medicine and automatic classification functions. DL algorithm is based on learning features from data by processing huge amount of data and extracting the meaningful patterns [4]. Multiple researches have been done on automated detection of diabetic retinopathy and most of them were performed SVMs or CNN. Torre et al [5] stated that DL has become very important as a new method of machine learning in recent years.

IX. DEEP LEARNING METHODS

Deep learning defines as neural networks with a great number of parameters and layers in one of the following network architectures:

a. Convolutional Neural Networks (CNN)

A Convolutional Neural Network (CNN or ConvNet) is a deep learning algorithm that was initiated by Kunihiko Fukushima. CNN algorithm can take in an input image and assign importance to different objects in the image to be able to distinguish one from the others. ConvNet is specializing in processing data that uses multiple layers such as convolutional layers, pooling layers and fully connected layer. The core building block of the CNN is convolutional layers which filter inputs to extract useful data for certain tasks. Whereas, pooling layers are used to maintain the process of efficiently training of the model by replacing the output of the network at definite locations for extracting dominant features for limited rotation and positional invariance. Furthermore, pooling layers decreases the memory consumption and the spatial size of the convolved feature and therefore permit more convolutional layers for usage [41].

b. Recurrent Neural Networks (RNN)

Recurrent Neural Networks, also known as RNNs which were initially proposed by Elman. RNN is a type of neural networks that comprises at least one feed-back connection and designed to process sequential data. RNNs models one of the most powerful type of neural network that have shown great results in various problems for example language modeling, speech recognition, image captioning, translation and etc. RNNs are called recurrent because they take a series of input and produce a series of output vectors and each output depended on the previous computations. In the process of recurrent neural networks, there is no predetermined limit on size [43].

c. Restricted Boltzmann Machine (RBM)

Restricted Boltzmann machine (RBMs) was primarily introduced by Paul Smolensky in 1986. RBM is a useful deep learning a network that can be employed to more interesting problems because of computational power and collaborative filtering. RBMs algorithm is useful for many domains such as regression, image classification, feature learning, denoising and etc. There are two main layers constitute the building blocks of RBM which are: the visible layer, and the hidden layer. RBM is considered as restricted because there is no intra-layer connection [45].

d. Autoencoders

Autoencoders are defined as an unsupervised learning method that don't use any labelled data. Autoencoders are directed neural network where the input layer is the same as the output layer. Autoencoders are usually include of input layers, output layers and hidden layers. This method takes a set of unlabeled inputs and tries to reconstruct them as correctly as possible after encoding them. As a result of this, the model decides what are the most important features in the present data [41].

X. DATASETS

Deep learning algorithms used various publicly available dataset to perform different tasks of models.

a. Kaggle dataset

Kaggle.com is the largest online community in the world for machine learning engineers which owned by Google LLC. and Kaggle community used by more than 220,000+ members. Kaggle.com has thousands of the publicly available datasets that are free to download. Different datasets are provided by Kaggle such as financial time-series, image datasets, CSVs, movie reviews, etc. Kaggle allow its member to acquire the datasets and used to build DL models in data science environment [52].

b. Messidor-2 dataset

Messidor-2 is a part of Messidor dataset which stands for Methods to Evaluate Segmentation and Indexing Techniques in the field of Retinal Ophthalmology. Messidor-2 dataset is a collection of fundus images that has been established to facilitate the studies for automated screening of diabetic retinopathy [44].

c. DRIVE dataset

DRIVE is stand for Digital Retinal Images for Vessel Extraction. DRIVE dataset was acquired from the program of DR screening in The Netherlands and has been established to enable studies on blood vessels segmentation in fundus images. The images that contained in the dataset were captured using a Canon CR5 non-mydriatic 3CCD camera at 768 by 584 pixels. All images in the DRIVE dataset were used actually for making clinical diagnoses [53].

XI. LIBRARIES

Python is programming language that used to build deep learning models with help of a popular libraries such as TensorFlow, NumPy, matplotlib, Keras, Theano. Some of these libraries are explained below:

a. TensorFlow

TensorFlow is an open source library for machine learning that developed by the Google Brain team in late 2015. TensorFlow is a Python library which offers APIs to develop applications with the framework in high-performance. TensorFlow is written in C++ and it's very fast at computing the matrix multiplication. TensorFlow is a collection of machine learning and deep learning algorithms and models that allow for flexible development environment. TensorFlow goes through a list of operations and takes input as a multi-dimensional array. TensorFlow is cross-platform that runs on GPUs and CPUs, including embedded platforms and mobile. The architecture of TensorFlow works in three areas which are data preprocessing, building model, and train and predict the model. The most important feature of TensorFlow is the TensorBoard that allows the user to monitor visually and graphically things such as model weights, learning rate, loss functions, etc. [39].

b. Keras

Keras is a python deep learning library that runs on top of TensorFlow as well as on top of Theano. Keras is adopted as a high-level API that used to build and train DL models. Keras is allowing for fast and easy prototyping of ML algorithms and supporting both recurrent networks and convolutional networks. Keras seamlessly runs on both GPU and CPU. The two main models of Keras are the sequential model and the model class [42].

c. Theano

Theano is key foundational library for DL in Python that was developed by the MILA-group in Canada at the University of Montreal. Theano was designed to handle numerical computation that needed for neural network algorithms that used in DL models. Theano can be used directly to build DL models that facilitate the process. Theano is a compiler for mathematical expressions that allows users for fast numerical computation, using multi-dimensional arrays [40].

XII. RELATED WORK

Gardner et al [10] used a CNN in their work to detect the features of DR in retinal images. The model was trained on 147 images that impacted by diabetes and 32 normal retinal images. They were able to detect diabetic retinopathy with a sensitivity of 88.4% and a specificity of 83.5%.

The study by Pratt et al [11] used a neural network to identify the features of DR in retinal images. The network was trained using GPU on Kaggle dataset to demonstrate impressive results. They achieved a 95% of sensitivity and a 75% of accuracy on the validation dataset of 5,000 fundus images. This study is claimed as one of the first papers that classify diabetic retinopathy into five grades.

Gulshan et al. [12] in their results, demonstrated that deep neural network can be trained. DL algorithm was trained using 128,175 fundus images acquired from EyePACS in the United States and fundus images from three hospitals in India. They reported high sensitivity and specificity for DR detection. In EYEPACS dataset, they achieved 97.5% sensitivity and 93.4% specificity, whereas for Messidor-2 set they achieved sensitivity of 96.1% and specificity of 93.9%. While, Voets M et al. [14] attempted to replicate the main method in the previous paper [12] by using availability public dataset of Kaggle (EyePACS) and Messidor-2. Due to inadequate details in the method description in that study, they were not able to get the same the results as reported. in their study, they reported AUC of 0.80 on Messidor-2 test-set and AUC of 0.94 on the EyePACS, whereas the original study achieved AUC of 0.99 on test-sets. The replicate study showed that selecting the suitable normalization method is very critical and is hence supposed to be used in the original study.

Hazim Johari et al [13] used Alexnet deep learning neural network on retinal images for DR detection by using availability public MESSIDOR database. They demonstrated that Alexnet layers is the perfect layer for deep learning. Their project achieved accuracy of 99.3% for training and 88.3% for the testing set.

Lin et al [15] in their work used deep learning to compare the performance of detection for severe diabetic retinopathy between entropy images and original fundus images. This study showed that using entropy images achieve 86.10%of accuracy, 73.24% of sensitivity, and 93.81% of specificity, whereas achieve 81.80% of accuracy, 68.36%of sensitivity, and 89.87%of specificity while using original fundus images. They established that transformed fundus photographs to entropy imaging can enhance the performance of deep learning and properly detect the referable DR.

Chandrakumar et al [17] proposed Deep Convolutional Neural Network (DCNN) solution that find better way to classifying the retinal images with little preprocessing techniques and might give high accuracy in DR classification. their proposed approach used available public databases such as Kaggle, DRIVE, STARE and achieved around 94% of accuracy for classifying DR stages.

Sayed et al [19] made use of two machine learning models in their work which are Probabilistic Neural Network (PNN) and Support vector machines (SVM) for detection of diabetic retinopathy. This study achieved 90% of accuracy of detection in SVM whereas 80% in PNN. Thereby they reported that SVM model is more efficient than PNN model.

Abramoff et al [21] in their study compare between the performance of automated detection of DR that employ a deep learning enhanced algorithm and the performance of Iowa Detection Program (IDP) that performed without deep learning components. DL algorithms for the automated DR detection achieved sensitivity of 96.8% and specificity of 87.0% whereas IDP published 94.4% - 99.3% sensitivity and 55.7% - 63.0% specificity. They reported that DL enhanced algorithm achieved significantly better performance and would enhance automated DR detection than IDP that does not employ DL algorithm.

Ari Mukti et al [22] presented in their paper an automatic grading system for DR using discrete curvelet transform (FDCT) features with SVM Classifier. The proposed system tested using retinal images from databases of Messidor and achieved 86.23% accuracy. Experiment results show that the proposed system could save effort and time.

XIII. COMPARISON OF PERFORMANCE OF DEEP LEARNING-BASED DR ALGORITHMS

According to the findings of latest previous studies on DR screening algorithms, the accuracy varied from 75 to 100%, the sensitivity from 57 to 100% and the specificity from 50 to 98% (Table 1). Based on the above results, we can say that most artificial intelligence methods will be able to detect diabetic retinopathy and would perform better and faster than ophthalmologists. Table 2 compares the performance of various studies that conducted for DR screening based on retina images using DL.

-based DR algorithms for Fundus images

S.No	Authors	Year	Dataset	Method	Sensitivity	Specificity	Accuracy
1	Chakrabarty [24]	2019	High-Resolution Fundus (HRF) Image Database	CNN	100%	-	100%
2	Hemanth et al. [25]	2019	MESSIDOR	CNN	94%	98%	97%
3	Thakar et al. [29]	2019	-	web application (Python Packages)	-	-	95% for optic disc elimination 56% for microaneurysms detection.
4	[Leeza et al. 32]	2019	-	dictionary-based approach (BoF), SVM, CNN	95.92%	98.90%	-
5	R. Sahoo and C. Sekhar [34]	2019	STARE, DRIVE, DIARETDB1 and DIARETDB0	Wavelet based Image segmentation	95.87%	96.2%	95.72%
6	Li et al. [26]	2018	Real images	CNN	92.5%	98.5%	-
7	Hijazi et al. [30]	2018	Messidor-2	CNN ensemble	99.0%	87.0%	-
8	Ari Mukti et al. [22]	2018	Messidor	SVM Classifier	-	-	86.23%
9	Hazim Johari et al. [13]	2018	MESSIDOR	Alexnet CNN	-	-	Training- 99.3%, Testing- 88.3%
10	Voets M et al. [17]	2018	Kaggle and Messidor-2	-	5.40%- Kaggle 57.60%Messidor2	55.40%- Kaggle 54.60%- Messidor-2	-
11	Lin et al. [15]	2018	Kaggle	CNN	73.24%	93.81%	86.10%
12	Ramachandran et al. [35]	2017	Otago database and Messidor international database	deep neural network	84.6% for Otago and with 96.0% for Messidor.	79.7% for Otago and with 90.0% for Messidor.	
13	Xu et al. [23]	2017	Kaggle	Deep CNN	-	-	94.5%
14	Sayed et al. [19]	2017	Real images	SVM, PNN	-	-	90% in SVM, 80% in PNN
15	(Rakhlin, 2019)	2017	Kaggle and Messidor-2	CNNs	Messidor-2- 99%	Messidor-2- 71%	-
16	Bhaskaranand et al. [33]	2016	EyePACS		90%	63.2%	-
17	Abramoff et al. [21]	2016	Messidor-2	DL enhanced algorithm	96.8%	87.0%	-
18	Chandrakumar et al. [17]	2016	Kaggle, DRIVE, STARE	DCNN	-	-	94%
19	Pratt et al. [11]	2016	Kaggle dataset	CNN	95%	-	75%
20	Gulshan et al. [12	2016	EYEPACS, Messidor	DNN	97.5%,96.1%	93.4%, 93.9%	-
21	Kansal et al. [27]	2016	HEI-MED	hybrid CS-ACO	98.7%	98.7%	98.6%
22	Kumar et al. [31]	2016	Regional Institute of Ophthalmology (RIO)		80%	50%	
23	Partovi et al. [28]	2016	Real images (30 images of retinopathy patients)	morphological function	76%	98%	97%
24	Gardner et al. [10]	1996	-	CNN	88.4%	83.5%	91.7%, 93.1% and 73.8%

XIV. CHALLENGES AND LIMITATION

DR screening algorithms Just like any automated system, contain some limitation even it works in powerful DL models. Obtaining images from different hardware or from different datasets not present on training stage, might occasionally result in reduced the accuracy. But this challenge can be circumvented by train the models on broader datasets or fine-tuning the model on the new data [38]. UzZaman and Bashir. [54] reported in their dissertation that the models could not be trained with dataset that have images larger size. The system would be able to work in dataset with a larger pixel to detect the problem more accurately if the memory size of the graphics card is increased. Maliha. et al, [55] used few amounts of fundus photographs and due that reason they found difficulties to classify DR accurately. Thus, to get accurate classification of DR and with high accuracy, should use large amount of data.

One of the most important challenge that faced AI-based technology is the clinical validation and real time deployment of DL models in clinical practice. Most of the studies used a publicly available dataset for training models. However, this challenge can be addressed by diversifying the dataset that will be used for training stage [4].

XV. CONCLUSION

Diabetic retinopathy is one of the complications of diabetes mellitus that occurs due to damage of blood vessels in the light-sensitive tissues in the back of the eye (retina). At early stages, symptoms of DR may not appear and cause simple problems on vision, but in advance stages can cause to blindness. Therefore, early detection of diabetic retinopathy is important to prevent loss sight. AI technology would act as an auxiliary assistant in screening of diabetic retinopathy and offer diagnostic support but on other hand, it cannot substitute the ophthalmologists' role in clinical diagnosis. This research work has offered a comprehensive view on the state-of-the-art DL based methods associated to diabetic retinopathy diagnosis and most of them shown that DL has impressive results of high accuracy in automated image analysis of retinal images. As AI technology evolves it would become more integrated into ophthalmic care and the ophthalmologists and physicians would requisite to learn how to use these technical advances with medical care.

REFERENCE

1. WHO | Diabetes mellitus", *Who.int*, 2019. [Online]. Available: https://www.who.int/mediacentre/factsheets/fs138/en/. [Accessed: 05- May- 2019].
2. F. Cold and E. Health, "Types of Diabetes Mellitus", WebMD, 2019. [Online]. Available: https://www.webmd.com/diabetes/guide/types-of-diabetes-mellitus#1. [Accessed: 05- May- 2019].
3. D. Singh Sisodia, S. Nair and P. Khobragade, "Diabetic Retinal Fundus Images: Preprocessing and Feature Extraction For Early Detection of Diabetic Retinopathy", Biomedical and Pharmacology Journal, vol. 10, no. 02, pp. 615-626, 2017. Available: 10.13005/bpj/1148.
4. R. Raman, S. Srinivasan, S. Virmani, S. Sivaprasad, C. Rao and R. Rajalakshmi, "Fundus photograph-based deep learning algorithms in detecting diabetic retinopathy", Eye, vol. 33, no. 1, pp. 97-109, 2018. Available: 10.1038/s41433-018-0269-y.
5. J. de la Torre, D. Puig and A. Valls, "Weighted kappa loss function for multi-class classification of ordinal data in deep learning", Pattern Recognition Letters, vol. 105, pp. 144-154, 2018. Available: 10.1016/j.patrec.2017.05.018.
6. [6]P. Grewal, F. Oloumi, U. Rubin and M. Tennant, "Deep learning in ophthalmology: a review", Canadian Journal of Ophthalmology, vol. 53, no. 4, pp. 309-313, 2018. Available: 10.1016/j.jcjo.2018.04.019.
7. W. Lu, Y. Tong, Y. Yu, Y. Xing, C. Chen and Y. Shen, "Applications of Artificial Intelligence in Ophthalmology: General Overview", Journal of Ophthalmology, vol. 2018, pp. 1-15, 2018. Available: 10.1155/2018/5278196.
8. N. Graham, Artificial Intelligence, Vol. 1076, Blue Ridge Summit: Tab Books, Philadelphia, PA, USA, 1979.
9. V. Gulshan et al., "Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs", JAMA, vol. 316, no. 22, p. 2402, 2016. Available: 10.1001/jama.2016.17216.
10. G. Gardner, D. Keating, T. Williamson and A. Elliott, "Automatic detection of diabetic retinopathy using an artificial neural network: a screening tool.", British Journal of Ophthalmology, vol. 80, no. 11, pp. 940-944, 1996. Available: 10.1136/bjo.80.11.940.
11. H. Pratt, F. Coenen, D. Broadbent, S. Harding and Y. Zheng, "Convolutional Neural Networks for Diabetic Retinopathy", Procedia Computer Science, vol. 90, pp. 200-205, 2016. Available: 10.1016/j.procs.2016.07.014.
12. V. Gulshan et al., "Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs", JAMA, vol. 316, no. 22, p. 2402, 2016. Available: 10.1001/jama.2016.17216.
13. M. Hazim Johari et al., "Early Detection of Diabetic Retinopathy by Using Deep Learning Neural Network", International Journal of Engineering & Technology, vol. 7, no. 411, p. 198, 2018. Available: 10.14419/ijet.v7i4.11.20804.
14. Voets M, Møllersen K, Bongo LA. Replication study: Development and validation of deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs. arXiv preprint arXiv:1803.04337. 2018. http://arxiv.org/abs/1803.04337.
15. G. Lin et al., "Transforming Retinal Photographs to Entropy Images in Deep Learning to Improve Automated Detection for Diabetic Retinopathy", Journal of Ophthalmology, vol. 2018, pp. 1-6, 2018. Available: 10.1155/2018/2159702.
16. S. Dutta, B. Manideep, S. Basha, R. Caytiles and N. Iyengar, "Classification of Diabetic Retinopathy Images by Using Deep Learning Models", International Journal of Grid and Distributed Computing, vol. 11, no. 1, pp. 99-106, 2018. Available: 10.14257/ijgdc.2018.11.1.09.
17. Chandrakumar T and R Kathirvel, "Classifying Diabetic Retinopathy using Deep Learning Architecture", International Journal of Engineering Research and, vol. 5, no. 06, 2016. Available: 10.17577/ijertv5is060055.
18. V. Chandore and S. Asati, "Automatic Detection of Diabetic Retinopathy using deep Convolutional Neural Network", International Journal of Advance Research, Ideas and Innovations in Technology, vol. 3, no. 4, pp. 633-641, 2017. Available: http://www.ijariit.com. [Accessed 9 May 2019].
19. S. Sayed, S. Kapre and D. Inamdar, "Detection of Diabetic Retinopathy using Image Processing and Machine Learning", International Journal of Innovative Research in Science, Engineering and Technology, vol. 6, no. 1, pp. 99-107, 2017. Available: http://www.ijirset.com. [Accessed 9 May 2019].
20. [20]B. Ramasubramanian and G. Prabhakar, "An Early Screening System for the Detection of Diabetic Retinopathy using Image Processing", International Journal of Computer Applications, vol. 61, no. 15, pp. 6-10, 2013. Available: 10.5120/10002-4864.
21. M. Abràmoff et al., "Improved Automated Detection of Diabetic Retinopathy on a Publicly Available Dataset Through Integration of Deep Learning", Investigative Opthalmology & Visual Science, vol. 57, no. 13, p. 5200, 2016. Available: 10.1167/iovs.16-19964.
22. F. Ari Mukti, C. Eswaran, N. Hashim, H. Chiung Ching and M. Uvaze Ahamed Ayoobkhan, "An automated grading system for diabetic retinopathy using curvelet transform and hierarchical classification", International Journal of Engineering & Technology, vol. 7, no. 215, p. 154, 2018. Available: 10.14419/ijet.v7i2.15.11375.
23. 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. Available: 10.3390/molecules22122054.
24. N. Chakrabarty, "A Deep Learning Method for the detection of Diabetic Retinopathy", in 2018 5th IEEE Uttar Pradesh Section International Conference on Electrical, Electronics and Computer Engineering (UPCON), 2019.
25. D. Hemanth, O. Deperlioglu and U. Kose, "An enhanced diabetic retinopathy detection and classification approach using deep convolutional neural network", Neural Computing and Applications, 2019. Available: 10.1007/s00521-018-03974-0.
26. Z. Li et al., "An Automated Grading System for Detection of Vision-Threatening Referable Diabetic Retinopathy on the Basis of Color Fundus Photographs", Diabetes Care, vol. 41, no. 12, pp. 2509-2516, 2018. Available: 10.2337/dc18-0147.
27. K. Kansal and E. Nishi, "Automated Detection of Exudates for Diabetic Retinopathy Screening in Fundus Images Using CS-ACO Optimization Approach", International Journal of Bio-Science and Bio-Technology, vol. 8, no. 3, pp. 323-340, 2016. Available: 10.14257/ijbsbt.2016.8.3.33.
28. M. Partovi, S. Rasta and A. Javadzadeh, "Automatic detection of retinal exudates in fundus images of diabetic retinopathy patients", Journal of Analytical Research in Clinical Medicine, vol. 4, no. 2, pp. 104-109, 2016. Available: 10.15171/jarcm.2016.017.
29. B. Thakar, S. Patel, V. Palod, A. Shetty, P. Hatode and J. Khanapuri, "Automatic Detection of Microaneurysms in Diabetic Retinopathy Using Python", SSRN Electronic Journal, 2019. Available: 10.2139/ssrn.3367665.

30. B. Hijazi, G. Quellec, M. Lamard, B. Cochener,"Automatic detection of diabetic retinopathy using jointly trained CNNs", Acta Ophthalmologica, vol. 96, no. 261, pp. 52-52, 2018. Available: 10.1111/aos.13972_184.
31. P. Kumar, R. Deepak, A. Sathar, V. Sahasranamam and R. Kumar, "Automated Detection System for Diabetic Retinopathy Using Two Field Fundus Photography", Procedia Computer Science, vol. 93, pp. 486-494, 2016. Available: 10.1016/j.procs.2016.07.237.
32. M. Leeza and H. Farooq, "Detection of Severity Level of Diabetic Retinopathy Using Bag of Features Model", IET Computer Vision, 2019. Available: 10.1049/iet-cvi.2018.5263.
33. M. Bhaskaranand et al., "Automated Diabetic Retinopathy Screening and Monitoring Using Retinal Fundus Image Analysis", Journal of Diabetes Science and Technology, vol. 10, no. 2, pp. 254-261, 2016. Available: 10.1177/1932296816628546.
34. R. Sahoo and C. Sekhar, "Detection of Diabetic Retinopathy from Retinal Fundus Image using Wavelet based Image Segmentation", International Journal of Computer Applications, vol. 182, no. 47, pp. 46-50, 2019. Available: 10.5120/ijca2019918775.
35. N. Ramachandran, S. Hong, M. Sime and G. Wilson, "Diabetic retinopathy screening using deep neural network", Clinical & Experimental Ophthalmology, vol. 46, no. 4, pp. 412-416, 2017. Available: 10.1111/ceo.13056.
36. Y. Singh, P. Kumar Bhatia and O. Sangwan, "A REVIEW OF STUDIES ON MACHINE LEARNING TECHNIQUES", International Journal of Computer Science and Security, vol. 1, no. 1, pp. 70-84, 2007. [Accessed 20 May 2019].
37. Y. Li, N. Yeh, S. Chen and Y. Chung, "Computer-Assisted Diagnosis for Diabetic Retinopathy Based on Fundus Images Using Deep Convolutional Neural Network", Mobile Information Systems, vol. 2019, pp. 1-14, 2019. Available: 10.1155/2019/6142839.
38. A. Rakhlin, "Diabetic Retinopathy detection through integration of Deep Learning classification framework", 2019.
39. TensorFlow", TensorFlow, 2019. [Online]. Available: https://www.tensorflow.org. [Accessed: 19- Jun- 2019].
40. Welcome — Theano 1.0.0 documentation", Deeplearning.net, 2019. [Online]. Available: http://deeplearning.net/software/theano/. [Accessed: 19- Jun- 2019].
41. M. COŞKUN, Ö. YILDIRIM, A. UÇAR and Y. DEMIR, "AN OVERVIEW OF POPULAR DEEP LEARNING METHODS", European Journal of Technic, vol. 7, no. 2, pp. 165-176, 2017. Available: 10.23884/ejt.2017.7.2.11 [Accessed 18 June 2019].
42. Home - Keras Documentation", Keras.io, 2019. [Online]. Available: https://keras.io. [Accessed: 19- Jun- 2019].
43. K. Du and M. Swamy, "Recurrent Neural Networks", Neural Networks and Statistical Learning, pp. 337-353, 2013. Available: 10.1007/978-1-4471-5571-3_11 [Accessed 18 June 2019].
44. H. Guillaume PATRY, "Messidor - ADCIS", ADCIS, 2019. [Online]. Available: http://www.adcis.net/en/third-party/messidor/. [Accessed: 18- Jun- 2019].
45. R. Harrison, "Continuous restricted Boltzmann machines", Wireless Networks, 2018. Available: 10.1007/s11276-018-01903-6.
46. More than 350,000 Omani diabetics in 2050", Online Atheer Newspaper, 2019. [Online]. Available: https://www.atheer.om/archives/22790/. [Accessed: 18- Jun- 2019].
47. Alwatan.com, 2019. [Online]. Available: http://www.alwatan.com/graphics/2001/April/20.4/heads/ot9.htm. [Accessed: 18- Jun- 2019].
48. Prevalence of diabetic retinopathy, proliferative diabetic retinopathy and non-proliferative diabetic retinopathy in Asian T2DM patients: a systematic review and Meta-analysis", International Journal of Ophthalmology, 2019. Available: 10.18240/ijo.2019.02.19 [Accessed 20 June 2019].
49. Care.diabetesjournals.org, 2019. [Online]. Available: http://care.diabetesjournals.org/content/diacare/suppl/2018/12/17/42.Supplement_1.DC1/DC_42_S1_2019_UPDATED.pdf. [Accessed: 20- Jun- 2019].
50. International Diabetes Federation - Facts & figures.", 2019. [Online]. Available: https://idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html. [Accessed: 20- Jun- 2019].
51. J. Tarr, K. Kaul, M. Chopra, E. Kohner and R. Chibber, "Pathophysiology of Diabetic Retinopathy", ISRN Ophthalmology, vol. 2013, pp. 1-13, 2013. Available: 10.1155/2013/343560 [Accessed 20 June 2019].
52. Kaggle: Your Home for Data Science", Kaggle.com, 2019. [Online]. Available: https://www.kaggle.com/. [Accessed: 18- Jun- 2019].
53. DRIVE: Digital Retinal Images for Vessel Extraction", Isi.uu.nl, 2019. [Online]. Available: http://www.isi.uu.nl/Research/Databases/DRIVE/. [Accessed: 18- Jun- 2019].
54. A. UzZaman and S. Bashir, "DIABETIC RETINOPATHY DETECTION USING IMAGE- PROCESSING", Master, BRACUniversity, 2016.
55. M. Maliha, A. Tareque and S. Saha Roy, "Diabetic Retinopathy Detection Using Machine Learning", Bachelor, Engineering BRAC University, 2018.
56. Diabetic Retinopathy - Middle East", American Academy of Ophthalmology, 2019. [Online]. Available: https://www.aao.org/topic-detail/diabetic-retinopathy-middle-east. [Accessed: 01- Jul- 2019].

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