Detection of Clinical Features for the Early Diagnosis and Classification of Diabetic Retinopathy : A Systematic Review

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Abstract**—** Diabetic retinopathy is the principal cause of vision loss in patients with diabetes. It is progressive eye disease that affects the retina's blood vessels, if not detected and treated at an early stage it can lead to loss of vision. Diabetic Retinopathy (DR) is the chronic diabetes which directly or indirectly affects the human vision. In its early stages, DR has no signs of disease or illness and the late diagnosis contribute to undeviating vision loss. Automatic retinal image analysis is emerging as an effective technique for the identification of diabetic retinopathy. The aim of this analysis is to provide an exhaustive review of the results of various algorithms available for diabetic retinopathy detection and classification. A total of 57 articles from 2015-2019 are analyzed in this study to identify different characteristics of diabetic retinopathy. Such techniques ' output is summarized by considering the AUC, precision, specificity and sensitivity with respect to the test data sets. The results of the performance comparison suggest that precise implementation of automated detection systems is still needed to assist in the clinical diagnosis of diabetic retinopathy.

Keywords: Diabetic Retinopathy; Microaneurysm; Exudate

I. INTRODUCTION

Diabetes is one of the complex diseases and is recognized as an incurable disease which quickly emerges as a global problem. Diabetes divided into two types, type I diabetes in which the body cannot produce insulin and type II diabetes in which the body cannot use insulin. The blood sugar level rises significantly in both cases. This leads to macrovascular complications, including cardiovascular disease, stroke, and peripheral artery disease, and neuropathy, nephropathy, and retinopathy can also be caused by microvascular complications. In diabetes patients, the microvascular complications caused by high glucose can affect human retina and lead to a retinal abnormality known as Diabetic Reti-nopathy (DR). DR is a common cause of blindness across the globe — before 50 years of age [2]. Diabetic Retinopathy (DR) is a progressive chronic, sight-threatening, diabetes-related retinal complication[3]. Diabetic retinopathy occurs when the blood vessels within the retina become weakened by diabetes, leaking blood and fluids into the tissue around. This leakage of fluid causes microaneurysms, hemorrhages, hard exudates and patches of cotton wool (a.k.a., soft exudates)[4],[5]. DR symptom is the presence of microaneurysms (MAs), are capillary swellings, which appear in retinal images as small dark red spots resulting in tiny leakage of the blood vessels in the retina. Microaneurysms play a key role in identifying diabetic retinopathy early on. Nevertheless, the risk of vision loss reduces with early DR diagnosis and ongoing treatment.

1.1 Diabetes Complications

Diabetes Mellitus (DM) is a series of metabolic infections with many side effects such as blood pressure, micro-vascular damage and macro-vascular complications such as retinopathy, neuropathy and nephropathy, cardiovascular disease risk, eye disease and chronic kidney disease.. A increasing body of evidence indicates that diabetes itself and some anti-diabetic treatments can increase the risk of cancer[6]. Most diabetic adults have at least one chronic co-morbid illness[7]. Many work is going on in this field and some of the statistics report indicates that most people will die due to the high level of glucose leading either to cancer or heart disease. The effects are uncontrolled and result in serious damage to many human body systems over time, especially for the nerves and blood vessels[7,8]. We have briefly discussed about thosefeatures.

Diabetic Nephropathy The major cause of end-stage renal diseases is diabetic nephropathy. As protein is digested by the body it contaminates the blood with waste products. These waste materials are taken out by the renals. An integral part of this filter is a large number of small blood vessels (capillaries). They start leak after 20-30 years, and useful protein gets lost in urine[9]. Interruption of the renin – angiotensin system has been reported to delay the development of renal diseases in patients with type 1 diabetes, but comparable data are not available for patients with type 2 [10].

Diabetic Cardiomyopathy Diabetes and the ischemic heart disease patients tend to have an elevated myocardial dysfunction leading to premature heart failure (diabetic cardiomyopathy). But diabetes patients are vulnerable to congestive heart failure[11].

Diabetic Neuropathy The consequence of diabetic neuropathy is a gradual loss of nerve function that limits the amount of sensation on the feet's plantar aspects[12]. This reduced sensation discourages people from experiencing the onset or termination of a foot injury. As a result, patients with this condition are more susceptible to plant ulceration[12]. People with DM can develop nerve problems at any given time

Diabetic Retinopathy There's increased chance of developing DR over the years after the onset of DM. DR is asymptomatic and goes unnoticed until it reaches the advanced stage, and a timely diagnosis is necessary with the assistance of better screening options and facilities[14]. Diabetic retinopathy characteristics(symptoms) Microaneurysms and neovascularisation, intraretinal hemorrhages, exudates, redlesion, perimeter, width and branching angles, etc. are important DR clinical, geometrical & haemodynamic features.

Diabetic retinopathy that is caused by changes in the blood vessels that nourish the retina. DR is narrowly categorized into non-proliferative DR (NPDR) and proliferative DR (PDR) based on the production of pathological characteristics. NPDR first occurs, and PDR is the advanced stage where new irregular blood vessels are formed. Possible treatment choices at the PD level. The treatment options available at the PDR stage, such as laser photocoagulation, anti-VEGF injection, intraretinal injection, and vitrectomy, are found to be less effective and do not retrieve the vision loss that has already occurred[15]. Early diagnosis of DR helps in vision loss and impairment prevention.

Various clinical features present through the different stages of DR are:

Microaneurysm (MA) : Microaneurysms (MAs) reflect deformations in blood vessel walls. They classified as " balloon-shaped deformations" due to hyperglycemia caused by permeability of the vasculature[16]. Many MAs is directly proportional to DR level or point. The area of MAs is 1-3 pixels is in different fundus image databases.

Haemorrhages (HEM) :Hemorrhages (HMAs) are created because the damaged capillaries leak blood. There are three categories of HMAs. They are: dot, flame and blot. The HMAs mark are mysterious spots. In color properties, these are hard to distinguish from MAs, but these are larger in size. Due to their flame shape Flame HMAs are distinguished . These are formed due to blood leakage and in alignment with the nerve fibers. "Blot HMAs" usually have irregular shape and larger in size[17].

Hard exudates : Strong exudates on the retina are artifacts of bright yellow or white colour. Such artifacts have waxy appearance from the blood vessels and sharp edges against the backdrop. Strong exudates are formed due to blood leakage from the veins, and exudates have circular shape around the vessels.

Soft exudates : Soft exudates or Cotton Wool Spots(CWS) occurs because of arteriole occlusion. The reduced blood flow to the retina causes Retinal Nerve Fibre Layer (RNFL) ischemia that affects the axoplasmic flow and causes axoplasmic debris to accumulate in retinal ganglion cell axons. The debris accumulation appears as fluffy white lesions in the RNFL called CWS.

Types and Stages of Retinopathy

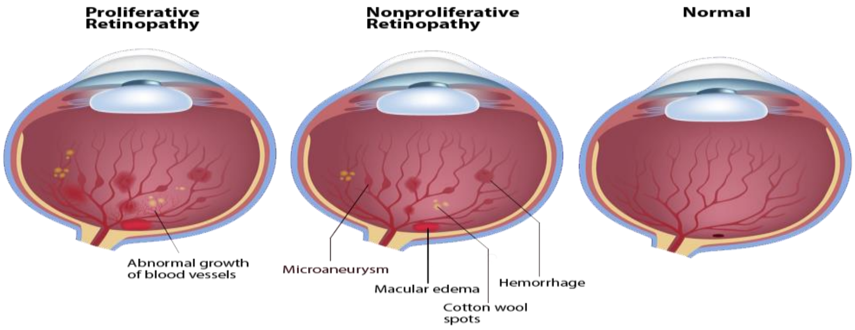
DR forms are based on blood vessel injury, number of MA and HMA at retina, and development of irregular new blood vessels. Stages of diabetic retinopathy depend on the existence of certain characteristics, and the severity / density of these characteristics[18]. The non-proliferative DR type is defined as normal, mild, moderate, and extreme in terms of sensitivity and number of MAs and HMAs

•*Normal*: If no DR sign is observed, this class is called Normal

•*Mild:* Only MAs are found in mild DR.

•*Moderate DR:* If the number of MAs, haemorrhages lesst han 20 in each quadrant, hard exudates white lesion, cotton wool.

• *Severe DR:* MAs, more than 20 haemorrhages in each quadrant, Venous beading in more than two quadrants, exudates, redlesion Neovascularization (NV), which is the development of irregular new blood vessels, characterizes the condition proliferates diabetic retinopathy(PDR). It is this ver stage of retinopathy and starting to grow new blood vessels anywhere in the eye. Therefore, MA and NV are two clinically important types of lesion[19] and fluid in DR is categorized as exudates and non-exudates[20].



1.2 *Performance Evaluation of classifier*

In most papers the parameters including True Positive(TP), False Positive(FP), TrueNegative(TN) and False Negative(FN) are measured using normal and abnormal data base photos. Such parameters are used in the estimation of the specificity (SP), sensitivity (SN) and accuracy (Acc) shown in equations (1), (2) and (3) respectively for a given image dataset.

1. Sensitivity is a measure of system which is calculated using the following equation.

Sensitivity = [TP/(TP+FN)] (1)

2. Specificity is a measure of system in which is calculated using the following equation.

Specificity = [TN/(TN+FP)] (2)

3. Accuracy is a measure of total number of well classified new vessel pixels and normal vessel pixels.

Accuracy = [(TP+TN)/(TP+FN+TN+FP)] (3)

II. MICROANEURYSMS DETECTION

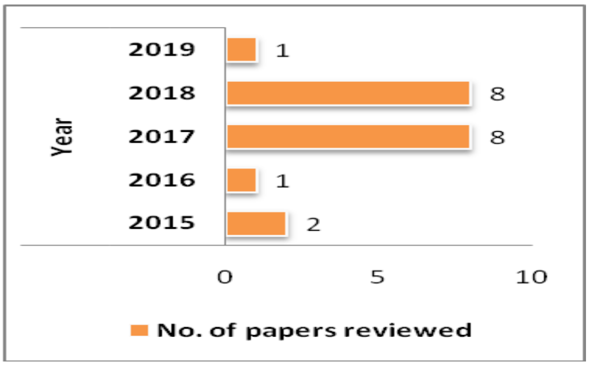
The study conducted by [21] Shilpa Joshi et al.(2019) Developed an automated detection system, the successful detection of the number of microaneurysms correlates with the stages of the retinal diseases and its early diagnosis. The approach of the optimal combination of preprocessing, morphological processing and feature based candidate extraction for MA detection shows that the proposed system is useful as automated MA detection systems for early diagnosis of DR. Similarly the study carried out by [22] Shailesh Kumar et al.(2018) proposed an improved scheme for the detection of diabetic retinopathy by accurate determination of number and area of microaneurysm. The achieved value of sensitivity and specificity shows that the proposed diagnostic system is better for non-proliferative diabetic retinopathy detection. The work carried out by [23] P Manohar et al.(2018) Proposed a simple approach to MA detection using mathematic morphology. The system provides the count of MAs necessary for automatic grading of the severity of DR. Similarly [24] Balazs Harangi et al.(2018) have proposed an ensemble-based neural network architecture for the recognition of MAs in fundus images. Our model connects different individual DCNNs to enable their simultaneous training. we also apply such deep convolutional neural network (DCNN) based techniques. The proposed method by [25] S.Sudha et al.(2018) is to bring to light the microaneurysms using image processing and to classify the severity of Diabetic Retinopathy. In this proposed system, the lesions are extracted by using graph cut segmentation and the support vector machine (SVM) classifier with PCA is applied to classify the severity of DR. [26] Mobeen ur Rehman et.al.(2018) proposed a novel approach to detect Diabetic Retinopathy disease using retinoscopy images. Pre-processed by histogram equalization. Wavelet Transform is used for Wavelet coefficients extraction from the images. KNN and SVM classifiers are used to identify the presence of Diabetic Retinopathy. Performance of the KNN and SVM were evaluated on the basis of correct detection(sensitivity), correct negation of false image (specificity), correct negation of non-DR (accuracy), It is clear from the study that SVM has surpassed KNN in sensitivity. [27] Yuji Hatanaka et.al.(2018) proposed a method structured with a two-step DCNN and three-layer perceptron with 48 features for false positives (FPs) reduction using deep convolutional neural networks (DCNN) have, this study conducts automated MA detection using DCNN shown superior performance in image recognition studies. [28] Priyanka Powar, et al.(2018) proposed an approach is to detect microaneurysms in retinal fundus image through segmentation followed by feature extraction in diabetic retinopathy disease. MAs detection with extracted features classified using k-means clustering and comparative study of algorithm and classification using support vector machine (SVM). Shape features of MAs are considered for better accuracy of detection. [29] The purpose of Wen Cao et al(2018) is to detect the microaneurysms using small 25 by 25 pixel patches extracted from retinal images which are directly fed as inputs to the classifiers and MA vs non-MA patches was performed using three sets of features for SVM, RF and NN. In addition two principal component analysis techniques are used for reducing the input dimensionality. With traditional machine learning methods and leave-10-patients-out cross validations SVM outperforms the RF and NN. [30] The aim of Arati Manjaramkar and Manesh Kokare(2017) is to detect Diabetic Retinopathy in early stages a novel two-level method morphology for MA candidate extraction and use of binary decision tree (DT) classifier and regression tree(CART) for true MA classification for DR detection, CART technique outperforms earlier state-of-the-art methods in terms of better classification results. [31] Lin Li, et al.(2017) presented an approach that can automatically detect regions that contain MA lesions. The approach first partitions a color fundus image into regions based on a region growing method starting from the pixel with the global maximum intensity. Then the approach extracts the features of each region and uses trained ANN to decide whether a region contains MA lesions. [32] Ling Dai, et al.(2017) proposed a framework performs favorably by overcoming MA detection challenges including unbalanced dataset and imaging conditions faced by the existing approaches, via multi-sieving training strategy and multi-modality information of clinical reports and visual features. [33] Diana Veiga, et al.(2017) have proposed a Laws texture features-based approach to detect MAs in colour fundus images. Combining Laws texture features with other more conventional features, such as region context, shape and intensity, resulted in an efficient approach for the final classification of MAs. This method proved that Laws texture features are adequate for detecting MAs' candidates, achieving sensitivities close to 100%. Specifically, a sensitivity of 99% was achieved for LaTIM, e-ophtha and ROC training, and a sensitivity of 97% was obtained for the ROC testing dataset. [34] E.Dhiravidachelvi, et al.(2017) have developed an approach to detect MA automatically and help ophthalmologist for pre-screening process. Automatic MA detection using CHT with SVM classification proved its performance via performance metrics such as Sensitivity is 97.5%, Specificity is 100% and its Accuracy in classification is 98%. an ACHT – [Automatic Circular Hugh Transform] method is applied to detect the circular shape of MA in a DRFI. The detect MA originality is investigated and evaluated using the feature extraction, classification by GLCM combined SVM, which compares shape model with the colour features. [35] Jen Hong Tan,et al.(2017) proposed to use a 10-layer convolutional neural network to automatically, simultaneously segment and discriminate exudates, haemorrhages and micro-aneurysms. Input image is normalized before segmentation. The net is trained in two stages to improve performance. [36] Sangita Bharkad,et al.(2017) work elaborates the new approach for detection of MAs in retinal images. This approach is tested on standard DIARETDB1 database. In this approach, shape and size based features are used for detection of MAs. [37] Sreng et al. (2017) developed an approach using canny edge and maximum entropy-based method to detect MAs from fundus images. A morphological operation followed by erosion was employed inorder to identify the MA pattern within image. Accuracy of 90% obtained after vesse removal, normalization and segmentatioon using canny edge and entropy methods to detect MA patterns. [38] Juan Shan, et al.(2016) A novel approach of two layer SSAE is presented for detection of MA. SMC classifier is used to detect MA lesions from fundus image eith complicated background. Performance comparison before and after tuning is done and after tuning gives the best result. [39] The main aim of Vineeta Das et al(2015) is to detect the microaneurysm by employing Shannon and Tsallis entropy thresholding in conjunction with Naïve Bayes classifier. The proposed method shows better performance to the existing methods. [40] Romero et al. in [2015] recommended bottom-hat and hit-or-miss transform methods for MA extraction after normalization of the gray contents of an image. To obtain an intact reddish region with a brighter part, a bottom-hat transformation was applied on the gray scale image. Blood vessel elimination was done using a hit/miss transformation application and finally, principal component analysis (PCA) and radon transform (RT) were applied to detect true MA points. They achieved a classification accuracy of 95.93%.

TABLE I. COMPARATIVE STUDY OF VARIOUS ALGORITHMS FOR DETECTION OF MICROANEURYSMS

Ref. No	Year	Authors	Preprocessing	Microaneurysms Det	DataBase	ACC	SP	SN
21	2019	Shilpa Joshi, et al.	median filtering, morphological processing, , Thresholding	Connected component analysis	Diaretdb1,	92	89.22	91
					e-ophtha		83	82
22	2018	Shailesh Kumar, et al.	Green channel, Adaptive histogram equalization (ADHE), Mathematical morphology operation, Grey scale conversion, CLAHE	SVM	DIARETDB 1		92 %	96 %
23	2018	P Manohar,et al.	median filter, morphological opening, closing and erosion operations, Green channel extraction, Contrast Limited Adaptive Histogram Equalization (CLAHE).	Rule-based classifier, mathematic morphology	DIARETB1		92.79	80.41
24	2018	Balazs Harangi, et al.	Stochastic gradient decent algorithm and Backpropagation algorithm	AlexNet-0.7934 0.9375 0.2400 GoogLeNet-0.8843, 0.9896 ,0.4800 VGGNet-0.7603, 0.7917, 0.6400 Ensemble-0.6942, 0.6458, 0.8800	e-ophtha-MA ROC DIARETDB 1 MESSIDOR	0.7934	0.9375	0.2400
25	2018	S.SUDHA,et al.	Green channel extraction , Adaptivehistogramequalization, Graph cut segmentation	SVM with PCA	Images taken from fundus camera		94.44	87.5
26	2018	Mobeen ur Rehman et.al.	Histogram Equilization, Discrete Wavelet Transform, Feature Extraction	KNN-98.16, SVM-97.85%	MESSIDOR	98.16		
27	2018	Yuji Hatanaka et.al.	Double ring filter, Gabor Filter and Shape index	DCCN (GoogLeNet),	DIARETDB 1		84 %	

			based on Hessian Matrix	SVM				
28	2018	Priyanka Powar, et al.	Gray scale conversion, morphological operations	K-means clustering, SVM	DIARETDB 1		92 .5 0	
29	2018	Wen Cao et.al.	Raw pixel intensities of extracted patches served directly as inputs	Random Forest Classifier, Neural Networks, Support Vector Machines	DIARETDB 1			
30	2017	Arati Manjaramkar and Manesh Kokare	Morphological Operations	Decision Tree(DT), Classification and Regression Tree(CART)	DIARETDB 1	98.6 %		
31	2017	Lin Li, et al.	blood vessel segmentation, region growing, thresholding technique	ANN classifier	DIARETDB 1	93.9		
32	2017	Ling Dai, et al.	histogram balance, Simple Linear Iterative Clustering (SLIC)	MS-CNN (AlexNet)	DIARETDB 1, local hospital images.	0.961		
33	2017	Diana Veiga, et al.	two-dimensional discrete stationary wavelet transform, Inverse Wavelet Transform, Median Filter	SVM	LaTIM, e-ophtha, ROC		99 % 97 97	
34	2017	E. Dhiravidachelvi , et al.	PT-[Pixel Transformation], CHT – [Circular Hough Transform], GLCM.	SVM	DIARETDB 1	98	97 .5	100
35	2017	Jen Hong Tan, et al.	Normalization, Segmentation	CNN	CLEOPATR A		0. 46 06	0.97 99
36	2017	Sangita Bharkad, et al.	Green Channel Extraction, contrast limited adaptive histogram equalization. gray scale morphological Top-hat transform, median filter	thresholding	DIARETDB 1		87 .5 %	
37	2017	Sreng S, Maneerat N, et al.	Images resized, noise removal and image enhancement using median filter and 2D wavelet transformation	Canny edge, threshold	DIARETDB 1	90		

38	2016	Juan Shan, et al.	--	Stacked Sparse Autoencoder (SSAE)+Softmax Classifier (SMC)	DIARETDB	91.38		91.60
39	2015	Vineeta Das et al.	Histogram Equalization, Matched Filtering, Shannon entropy, Tsallis entropy thresholding	Naïve Bayes classifier	ROC,		58.28	
					DIARETDB 1		57.6	
40	2015	Romero et al.	An average gray value and its standard deviation, morphological opening operation for ROI extraction	PCA and RT	DIARETDB 1, ROC	95.93		



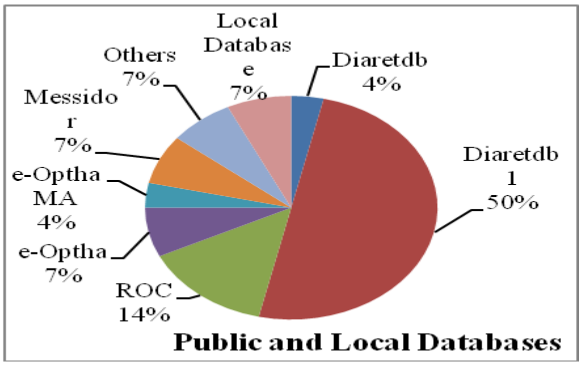


Figure 1 . Year wise No. of papers reivewed Figure 2. Percentage contibution of public and local Databases

III. EXUDATE DETECTION

The study proposed by [41] Anoop Balakrishnan Kadan, et al. (2019) is the prediction approach to predict automatically the early signs of diabetic retinopathy termed as hard exudates. The discrimination between exudates and non-exudate pixel is done with the feature sets such as colour and texture. Compare the approach with state-of-art classifiers the proposed approach provides better performance while. [42] Shengchun Long, et al.(2019) have developed and evaluated an automatic retinal image processing algorithm for HE detection using dynamic threshold and fuzzy C-means clustering (FCM) followed by support vector machine (SVM) for classification and the classifier SVM gave better accuracy. [43] Niladri Sekhar Datta, et al.(2019) a mathematical morphology based image processing technique is presented for the identification of Hard Exudates in retinal images. The outcome of the proposed pre-processing scheme is encouraging and also success rate increases for the identification of Hard Exudates. [44] Avula Benzamin et al.(2018) proposed an approach to detect hard exudates for detecting retinopathy in an early stage using deep learning method. [45] Anitha Gnanaselvi J et al.(2018) objective is to develop a model to detect Exudates in retinal fundus images using Convolutinal neural networks. This work provides an automatic image processing techniques to diagnose Exudates in human eye. [46] Worapan Kusakunniran, et al.(2018) proposed the method to segment the early signs of diabetic retinopathy called as hard exudates. The proposed method begins with using the MLP supervised learning to train the model of hard exudates detection. The model is then used to detect hard exudates in the testing retinal image. [47] Parham Khojasteh, et al.(2018) The novelty of this work is that it has compared different deep-learning approaches for automatic detection of exudate based on the experimentally obtained accuracy, sensitivity, and specificity. It has shown that "Resnet-50 +SVM" is the best among these for automatic detection of exudates in the fundus images, especially the sensitivity, which is important for medical diagnostics. [48] M. Moazam Fraz. et al.(2017) Proposed a novel approach for localization and segmentation of exudates in retinal fundus image using ensemble classifier of bagged decision tree. [49] Wei zhou, et al. (2017) have developed a superpixel multi-feature classification method for automatic detection of exudates. A supervised multi-variable classification algorithm is introduced in order to distinguish the true exudates from spurious exudates. Total 20 features were used among them 19 are intensity feature with SN-87.56, Sp-94.65 and AUC-96.03. One contextual feature with SN-87.12, SP-94.01 and AUC-95.87. For all features SN-88, SP-95 and AUC-96.55 were used to characterize these candidates. [50] Ambaji S. Jadhav et al.(2017) presented an effective approach for early detection of diabetic retinopathy by detection of exudates from color retinal image by using discrete wavelet transform and feature extraction. [51] Mario Canche, et al.(2017) have proposed an automatic method for hard exudates detection in Diabetic Retinopathy images. A new methodology for the automatic detection of exudate lesions was presented with the Adaboost Color algorithm. [52] R. Vanithamani, et al.(2017) designed a novel approach for the detection of exudates to diagnose DR. The entropy based segmentation method segments the exudates precisely and clearly by eliminating the blood vessels and optic disc from the fundus images. The proposed method SVM classifier gives better accuracy compared to SCG-BPN and GRN. [53] Shuang Yu, et al.(2017) have proposed a deep convolutional neural network (CNN) to achieve pixel-wise exudate identification. A set of exudate candidates are first extracted with morphological ultimate opening techniques and then the candidate points are passed to the trained CNN deep networks for classification. The method achieved a high pixel-wise accuracy for the training and test set. [54] Elaheh Imani et al.(2016) developed a novel method for exudates detection from retinal image using Morphological Component Analysis and the performance is better than the most of the state-of-art methods. [55] Qing Liu, et al.(2016) presented a location-to-segmentation strategy for automatic exudate segmentation in colour retinal fundus images, evaluated the method both at exudate-level and image-level using random forest classifier. [56] B V Shilpa, et al.(2016) a novel ensemble approach is proposed to automatically detect exudates in the fundus images. Morphological operations combined with logical operations is the ensemble approach that has enhanced the detection and marking of exudates. [57] Khin Yadanar Win, et al.(2016) proposed the accurate and efficient algorithm to localize the optic disc and detect exudates automatically from fundus retinal images by applying histogram analysis. Without the presence of the optic disc, exudates can be detected easily by using the histogram based thresholding technique. [58] P.R. Asha and S. Karpagavalli(2015) proposed work, the existence or lack of retinal exudates are identified using Extreme Learning Machine(ELM). To discover the occurrence of exudates features like Mean, Standard deviation, Centroid and Edge Strength are taken out from Luv color space after segmenting the Retinal image. A total of 100 images were used, out of which 80 images were used for training and 20 images were used for testing. [59] Hanung Adi Nugroho, et al.(2015) proposed method that successfully detects exudates and is useful to assist the ophthalmologists in analysing retinal fundus image especially for exudates detection to diagnose diabetic retinopathy. [60] T.Jaya et al.(2015) presented an expert decision making system designed using a fuzzy support vector machine (FSVM) classifier for the detection of hard exudates in fundus images. [61] T. Ruba, et al.(2015) developed an automated and simple method to detect exudates from non-dilated, low contrast retinal images. The performance of the process is measured using Specificity, sensitivity and accuracy. The proposed classifier results in 82% of accuracy. The proposed method for OD segmentation results in 99.63% of accuracy and the proposed method for Exudates segmentation results in 99.35%.

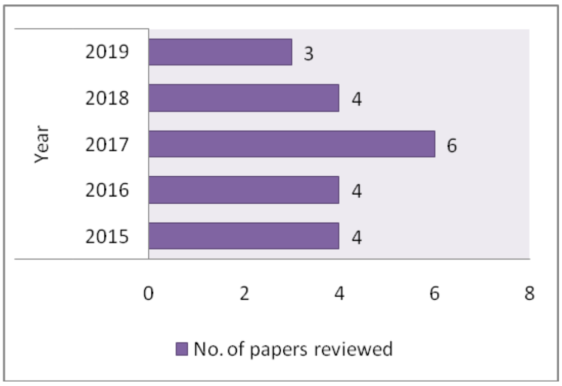
TABLE II. COMPARATIVE STUDY OF VARIOUS ALGORITHMS FOR DETECTION OF EXUDATES

Ref .No	Year	Authors	Preprocessing	Exudate Detection Algorithms	DataBase	ACC	SN	SP	AUC
41	2019	Anoop Balakrishnan Kadan, et al.	Gray scale conversion, Adaptive Median Filter, Enhances Guassian Mixture Model(EGMM), Adaptive Histogram Eqilization, Thresholding	KNN	DIARETDB1, DRIVE	99.34 %			

42	2019	Shengchun Long, et al.	Color intensity normalization and contrastenhancement, contrast limited adaptive histogram equalization (CLAHE), morphological opening	Dynamic threshold and FCM followed by an SVM for classification.	DIARETD B1, e-ophtha EX	SVM-97.7			
43	2019	Niladri Sekhar Datta, et al.	Fuzzy histogram, RGB to YCBCR conversion, Dynamic Histogram Equalization (DHE)	mathematical morphological operation	e-ophtha EX	--	98.67	98.89	0.972
					DIARETD B1	--	98.57	98.91	0.982
44	2018	Avula Benzamin et al.	Maxpool Operations	Tensorflow Deep Learning	IDRiD	98.6	-	-	-
45	2018	Anitha Gnanaselvi J et al.	Gray scale conversion, Gaussian filtering, thresholding	SVM	STARE	93.87	94.20	96.32	
				KNN		93.7	93.03	94.60	
				CNN		98	96	99.68	
46	2018	Worapan Kusakunniran, et al.	color transfer	MLP	E-Ophtha EX , DIARETD B1	0.998			
47	2018	Parham Khojasteh, et al.	--	CNN ResNet-50+KNN ResNet-50+OPF ResNet-50+SVM DRBM	DIARETD B1	98.2			
					e-Ophtha	97.6			
48	2017	M. Moazam Fraz. et al.	Morphological closing, histogram normalization, gabor filter application, adaptive thresholding, morphological reconstruction and top-hat filtering	Bagged Decision Tree (Ensemble Classifier Bagging+Decision Tree)	DIARETD B1	0.8772	0.9242	0.8125	0.9310
					e-optha EX	0.8925	0.8120	0.9460	0.9403
					HEI-MED	0.9577	0.9463	0.9641	0.9842
					Messidor	0.9836	0.9231	0.9903	0.9961
49	2017	Wei zhou, et al.	Global and local luminosity and contrast enhancement approach	Superpixel Multi-feature classification	DIARETD B1,e-optha EX	-	88	95	96.55
50	2017	Ambaji	gray scale conversion, median	Discrete	STARE,	-	95.3	100	-

		S. Jadhav et al.	filter, Adaptive histogram equalization, thresholding, mathematical morphology	Wavelet Transformation	DRIVE		2		
51	2017	Mario Canche	gray scale conversion:, median filter, wavelet transform and mathematical morphology	Fisher Discriminant Ratio (FDR), Adaptive Boosting	DIARETDB1	0.9412			
52	2017	R. Vanithamani, et al.	Entropy filtering, Grey Level Co-occurrence Matrix (GLCM), morphological opening	Support Vector Machine (SVM) - 96 , Scaled Conjugate Gradient Back Propagation Network (SCG-BPN) – 93.3 and Generalized Regression Neural Network (GRN) - 86 .	Diaretdb 1	96			
53	2017	Shuang Yu, et al.	morphological ultimate opening techniques	CNN	E-Ophtha EX	91.92			
54	2016	Elaheh Imani et al.	Green Channel Extraction, Ostu Thresholding morphological operations.	Marphological Component Analysis(MCA) algorithm.	DiaretDB		89.01	99.93	0.961
					Heimed		81.26	99.81	0.948
					e-optha		80.32	99.83	0.937
55	2016	Qing Liu et.al	Gaussian filter, Otus methods, thresholding	Random Forest Classifier	e-ophtha EX	76	76	75	
					DIARETDB1	79	83	75	
56	2016	B V Shilpa, et al.	Grayscale conversion, histogram equalization, Canny edge detection, guassian filtering,	Morphological Operations + logical operations	DIARETDB1, Forus health private limited.	-	100	89.6	0.969
57	2016	Khin Yadanar Win, et al.	histogram matching, green channel, Otsu thresholding	histogram based thresholding technique.	DRIVE, DIARECTDB1, STARE, and images from local	92%			

					dataset				
58	2015	P.R. Asha and S. Karpaga valli	optic disc removal, HSV color space conversion, local contrast enhancement and histogram specification are performed	extreme learning machine (ELM).	DIARETD B0DIARE TDB1	90%			
59	2015	Hanung Adi Nugroho , et al.	Green Channel Extraction, CLAHE, contrast stretching and median filtering, Butterworth high pass filtering (BHPF).	thresholding and morphological operations.	DIARETD B1	99.99 %			
60	2015	T. Jaya	morphological operations , edge-based techniques and based on circular Hough transform	SVM - 89.2 fuzzy support vector machine (FSVM) - 93.0	Images from Canon CR6-45NM digital imaging system	93.0%			
61	2015	T.Ruba	resizing images, Filtering image, median filter	SVM	MESSIDIOR	82%			



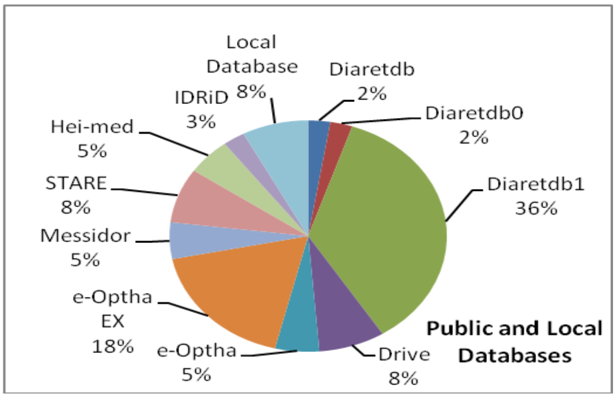


Figure 3. Year wise No. of papers reivewed Figure 4. Percentage contibution of public and local databases

IV. DR SCREENING AND STAGE CLASSIFICATION

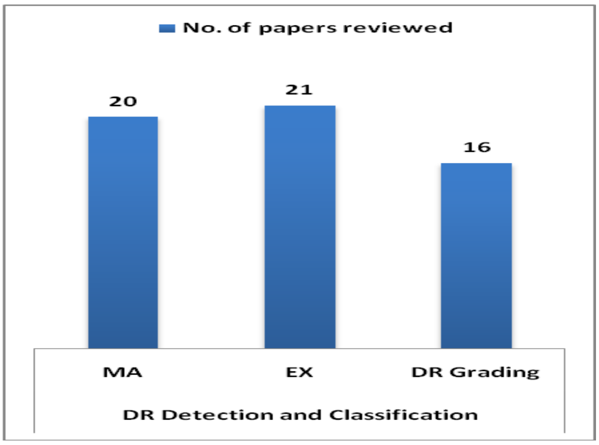
The work carried out by [62] Mohamed M. Adly et al.(2019) for grading the DR severity stages based on a Binarytree-based multiclass classifier of Convolutional Neural Networks (CNN) is presented. We proposed constructing the ensemble based on a criterion derived from the confusion-matrix values between any two successive DR stages. [63] Muhammad Mateen, et al.(2019) presented DR classification system achieves a symmetrically optimized solution through the combination of a Gaussian mixture model (GMM), visual geometry group network (VGGNet), singular value decomposition (SVD) and principle component analysis (PCA), and softmax, for region segmentation, high dimensional feature extraction, feature selection and fundus image classification, respectively. [64] Chunyan Lian, et al. (2018) We investigate four factors of employing deep CNN to DR classification problem, including network architectures, preprocessing, class imbalance and fine tuning. It is evident from the results that the VGG architecture fine-tuned from ImageNet, with image preprocessing and addressing class imbalance performs quite better than others. [65] Arkadiusz Kwasigroch, et al.(2018) proposed automated diabetic retinopathy screening framework. We have employed the deep convolutional neural networks to assess the proper stage of diabetic retinopathy based on color fundus photo of retina. leverage CNN networks to diagnose the diabetic retinopathy and its current stage, based on analysis of the photographs of retina. [66] Deepthi K Prasad, et al. (2018)

proposes an automated method for multistage classification of DR using Random forest classifier. images are classified as normal, mild-NPDR, moderate-NPDR and PDR depending on the severity level of the disease. An accuracy of 91.2% is obtained with the average precision and recall values being 0.908 and 0.912 respectively. The proposed method outweighs the earlier methods described in the literature in terms of increased accuracy. [67] Mobeen ur Rehman, et al. (2018) retinoscopy images were processed using wavelet transform. KNN and SVM were used to classify the retinoscopy images. proposed a methodology to detect Diabetic Retinopathy disease in early stages using retinoscopy images. [68] Pedro Costa, Adrian Galdran, et al.(2018) a new methodology based on the Multiple Instance Learning (MIL) framework is developed in order to overcome this necessity by leveraging the implicit information present on annotations made at the image level. Contrary to previous MIL-based DR detection systems, the main contribution of the proposed technique is the joint optimization of the instance encoding and the image classification stages. [69] Xiaoliang Wang, et al. (2018) A group of deep Convolutional Neural Network methods have been employed for DR stage classification. State-of-the-art accuracy result has been achieved by InceptionNet V3, which demonstrates the effectiveness of utilizing deep Convolutional Neural Networks for DR image recognition. [70] Smitha M, et al. (2018) Proposes a procedure for assessing the degree of severity of diabetic retinopathy. In order to help ophthalmologists diagnose the disease, it uses nondilated retinal fundus picture. The classifiers SVM and ELM were used to classify image input. The picture is categorized into normal or abnormal. Such classifiers are again used to classify the irregular images into mild or extreme.The average classification accuracy for the ELM is 94.76%. [71] Rishab Gargeya, et al. (2017) developed a robust diagnostic technology to accurate, robust and automatically detect the diabetic retinopathy using deep learning methods with a large scale data set. [72] Enrique V. Carrera, et al. (2017) main goal is to automatically classify the grade of non-proliferative diabetic retinopathy at any retinal image. The proposed features show a great potential for DRNP detection and classification. SVM can detect DRNP with a sensibility of almost 95%, while DRNP can be classified with an average accuracy of 85%. SVM consistently shows better results that other machine learning algorithms. [73] Saleh E, et al. (2017) a novel approach is proposed for diabetic retinopathy risk assessment using ensemble classifier Fuzzy Random Forests(FRF) and Dominance-based Rough Set Balanced Rule Ensemble (DRSA-BRE) based on electronic health records. The specificity and sensitivity obtained over 80%. [74] Arati Manjaramkar and Manesh Kokare (2017) developed an approach to detect Diabetic Retinopathy in early stages a novel two-level method morphology for MA candidate extraction and use of binary decision tree (DT) classifier and regression tree(CART) for true MA classification for DR detection, CART technique outperforms earlier state-of-the-art methods in terms of better classification results. [75] Varun Gulshan, Lily Peng, et al.(2016) ,an algorithm based on deep machine learning had high sensitivity and specificity for detecting referable diabetic retinopathy. For automated detection of diabetic retinopathy and diabetic macular edema in retinal fundus photographs. [76] Harry Pratta, Frans Coenen, et al. (2016) propose a CNN approach to diagnosing DR from digital fundus images and accurately classifying its severity. We develop a network with CNN architecture and data augmentation which can identify the intricate features involved in the classification task such as micro-aneurysms, exudate and haemorrhages on the retina and consequently provide a diagnosis automatically and without user input. [77] Valliappan Raman, Patrick Then and Putra Sumari(2016) is to detect the presence of abnormality features from retinal fundus images and classify different stages of diabetic retinopathy applying machine learning techniques The proposed methodology strengths of the proposed system are accurate feature extractions and accurate grading of non proliferative diabetic retinopathy lesions. Hence the proposed system gives more accurate classification and grading of retinal images.

TABLE III. COMPARATIVE STUDY OF VARIOUS ALGORITHMS FOR DETECTION AND CLASSIFICATION OF DIABETIC RETINOPATHY

Ref. No	Year	Authors	Preprocessing	DR Grading	DataBase	ACC	SN	SP	AUC
62	2019	Mohamed M. Adly	Gaussian filter, Gray Scale Conversion, illumination equalization	multiclass classifier	EyePACS	74			
				BinaryTree-based classifier		83.17	81.8	89.3	
63	2019	Muhammad Mateen	grayscaleconversion	VGGNet, FC7-V-PCA	KAGGLE	92.21			
				FC7-V-SVD		98.34			
				FC8-V-PCA		97.96			

				FC8-V-SVD		98.13			
64	2018	Chunyan Lian	Gaussian filter	CNN AlexNet	EyePACS	73.19			
				ResNet-50		76.41			
				VGG		79.04			
65	2018	Arkadiusz Kwasigroch	Standard minibatch Gradient Descent algorithm	DeepCNN	EyePACKS	82			
66	2018	Deepthi K Prasad	median filter, CLAHE	Random forest classifier	DIARETDB1, MESSIDOR	91.2			
67	2018	Mobeen ur Rehman	Histogram equalization	KNN	MESSIDOR	98.16	97.23	98.36	
				SVM		97.85	98.47	95.54	
68	2018	Pedro Costa	CLAHE, CE	MIL based BoVW	MESSIDOR				90
					DR1				93
					DR2				96
69	2018	Xiaoliang Wang		CNN AlexNet	Kaggle dataset	37.43			
				VGG16		50.03			
				InceptionNet V3		63.23			
70	2018	Smitha M	HSV color space, median filter, CLAHE	ELM	MESSIDOOR	94.76			
71	2017	Rishab Gargeya		Gradient Boosting Classifier	EyePACS				0.97
					Messidor				0.94
					E – Optha				0.95
72	2017	Enrique V. Carrera		SVM	Messidor		95		
73	2017	Emran Saleh		FRF	SJRUH (data from hospital)	80.29	80.67	80.18	
				DRSA		77.32	76.89	77.43	
74	2017	Arati Manjaramkar and Manesh Kokare	Morphological Operations	Decision Tree(DT), Classification & Regression Tree(CART)	DIARETDB1	98.6 %			
75	2016	Varun Gulshan		Inception-v3	EyePACS		90.3	98.1	0.991
					Messidor		87.0	98.5	0.990
76	2016	Harry Pratta	OpenCV	CNN	Kaggle	75	95		
77	2016	Valliappan Raman, Patrick Then and Putra Sumari	Contrast-limited Adaptive Histogram Equalization (CLAHE), Morphological operation	ANN classifier	DIARETDB0, DRIVE				



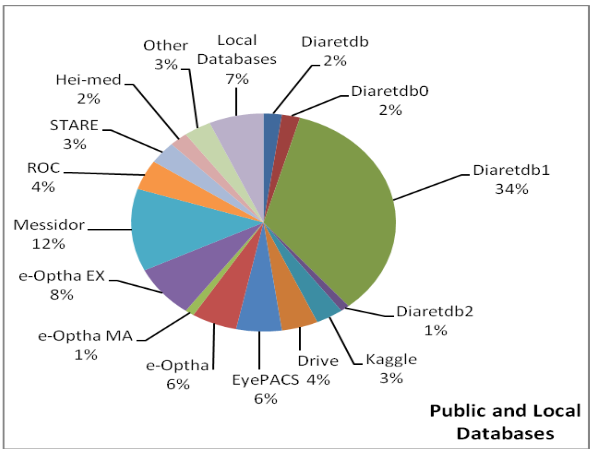


Figure 5. Year wise No. of papers reivewed for Figure 6. Percentage contibution of public and local databases

DR detection and Classification

V. DISSCUSSION

A common complication of diabetes is diabetic retinopathy. Diabetic retinopathy is classified as non-proliferative retinopathy (NPDR) & proliferative retinopathy (PDR). NPDR has two types of retinal lesions, namely microaneurysms and exudates. PDR relies on the network of the Vascular. Detection of microaneurysms is difficult because of the special characteristics of the these in terms of colour, shape and size. The eye's retina has some similar objects to the shape and size of microaneu-rysms, which makes it harder to diagnose properly. The development of microaneurysms results in haemorrhages progess towards exudates as a result prolonged chronic diabetes. Such clinical features in effect will result in severe vision loss or blindness unless treated early. The techniques for the preprocessing of images play an important role in order to increase the quality of fundus images which are to be used by the system.

Although considerable achievements have been made in retinal image analysis there is still room for finding the best algorithm which surpasses all in terms of accuracy. The proposed methods should bear minimum false –ves. The efficiency of overall system is the need and each step in it should ensure high sensitivity and specificity of the proposed algorithm. The literature showcases various techniques proposed by several researchers and also refinement made by few others to increase accuracy of algorithm. The only limitation is CNN training is time consuming and still challenging. Few research papers made emphasis on mathematical morphology, region growing and wavelet based methods. With basic image processing methods it was good initiative but issues like size of structuring element which varies the size of lesion, large number of false +ves still remain. Another approach includes candidate extraction, feature selection and classification. It is indeed difficult to identify the best algorithms and get efficient throughput. There are many emerging areas for research like deep learning with minimal training time, dictionary learning for specific lesions, findings best features and robust classifiers to attain highest FOC scores and accuracy.

VI. CONCLUSIONS

Automatic detection of clinical features of DR would be beneficial for diabetic retirement nopathy screening. There are several algorithms in the literature that can help the ophthalmologist test Diabetic Retinopathy in a simple computer-aided screening. The approach is considered best when fast, cost-effective, reliable and accurate.

All of these restrictions are time requirements. In medical image analysis the area of machine learning and image processing plays an important role. Precise identification of diabetic features needs a lot more focus to reduce the risk of serious vision failure significantly. The results of the algorithms reviewed are tested on various standard as well as some local databses. These results indicate that still there is need for accurate screening methodology, which in turn can save the vision loss by early detection of microaneurysms.

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