ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 10, Issue 4, 2017

Online - 2455-3891
Print - 0974-2441

Review Article

UNRAVELLING DIABETIC RETINOPATHY THROUGH IMAGE PROCESSING, NEURAL NETWORKS, AND FUZZY LOGIC: A REVIEW

SUDHA S*, SRINIVASAN A

Department of Electronics and Communication Engineering, Srinivasa Ramanujan Centre, SASTRA University, Kumbakonam, India. Email: mcvsudha@src.sastra.edu

Received: 10 January 2016, Revised and Accepted: 30 January 2017

ABSTRACT

One of the main causes of blindness is diabetic retinopathy (DR) and it may affect people of any ages. In these days, both young and old ages are affected by diabetes, and the diabetes is the main cause of DR. Hence, it is necessary to have an automated system with good accuracy and less computation time to diagnose and treat DR, and the automated system can simplify the work of ophthalmologists. The objective is to present an overview of various works recently in detecting and segmenting the various lesions of DR. Papers were categorized based on the diagnosing tools and the methods used for detecting early and advanced stage lesions. The early lesions of DR are microaneurysms, hemorrhages, exudates, and cotton wool spots and in the advanced stage, new and fragile blood vessels can be grown. Results have been evaluated in terms of sensitivity, specificity, accuracy and receiver operating characteristic curve. This paper analyzed the various steps and different algorithms used recently for the detection and classification of DR lesions. A comparison of performances has been made in terms of sensitivity, specificity, area under the curve, and accuracy. Suggestions, future work and the area to be improved were also discussed.

Keywords: Diabetic retinopathy, Image processing, Morphological operations, Neural network, Fuzzy logic.

 DOI: http://dx.doi.org/10.22159/ajpcr.2017.v10i4.17023

INTRODUCTION

In India, over 415 million people are affected by diabetes out of them over 50% of people may be affected by diabetic retinopathy (DR). DR can be diagnosed by clinical testing and automation. In clinical testing, the ophthalmologists will do clinical test and patients have to go for regular medical check-up. Moreover, it is time-consuming whereas in automation self-testing and diagnosing can be done. Patients may go for medical follow-up if it is really needed. However, automation consumes less time and it is less expensive. Many research papers have come with automation so the authors would like to categorize these papers based on the techniques used for the extraction of various lesions and classification.

Image processing is widely used to detect lesions in DR. Pre-processing, processing and classification are the three major steps in DR. For processing and classification IP, neural network (NN) and fuzzy logic have been used. Papers were categorized based on the diagnosing tools such as image processing, NN, and Fuzzy logic. Many papers have come up with the segmentation of retinal vasculature but only less have come for the detection of fovea and macula. This review paper can motivate researchers to identify the area where the research is to be improved.

IMAGE PROCESSING

Kumar *et al.* in 2016 have classified [1] retinal image as normal or DR image using two image fields per eye, one fovea centric and the other disc-centric. It was implemented as a four-stage process: (1) Retinal images were normalized, (2) optic disc and blood vessels (BVs) regions located automatically, (3) red and white lesions were extracted, and (4) The classification of the retina as DR or non-DR based on an aggregate of the lesions. Pre-processing includes I mage resizing by bi-cubic interpolation and brightness correction in HSV space. Multi-level wavelet decomposition and recursive region growing, histogram analysis, three stage intensity transformation, and multilevel histogram analysis were the processing. Liu *et al.* in 2016 have proposed [2] an algorithm for exudates (EXs) segmentation consisted of three stages anatomic structure removal, EX location and EX segmentation. Pre-processing includes field of view segmentation. Matched filters based BV segmentation, saliency-based optic disc segmentation and EX segmentation were the processing steps.

Kumar *et al.* in 2016 have attempted [3] to extract EXs regions by pre-processing (RGB to HIS conversion, noise removal by median filtering and adaptive histogram equalization) OD elimination, EXs segmentation using K-means clustering, feature extraction based on texture and colour using gray-level co-occurrence matrix (GLCM), feature selection by genetic algorithm, feature classification by probabilistic NN (PNN) classifier. Besenczi *et al.* in 2016 have reviewed the set of algorithms [4] used for image pre-processing, localization and segmentation of anatomical components and the detection of lesions. The authors personally suggested the following things: Parallel and spatial domain processing, stochastic optimization for setting free parameters and detected components and relations may be processed by graph algorithms to increase efficiency and to reduce the computation time.

Wu *et al.* in 2016 have proposed novel method [5] to detect microaneurysms (MAs). There were 27 characteristic features which contained Local and profile features. Authors used three classifiers for classifying candidates as MAs and non-MAs but found K-nearest neighbors (KNN) would be the best. Pre-processing includes illumination equalization, CLAHE enhancement and smoothing. Peak detection and region growing were used for candidate extraction.

In 2016, Bharkad has detected and segmented optic disc [6] using an equiripple finite impulse response (FIR) low-pass filter (LPF) and gray-scale morphological dilation and median filtering, respectively. Pre-processing includes adaptive histogram equalization and equiripple low pass FIR filtering. For OD detection maximum intensity pixels were extracted and thresholding. Srivastava *et al.* in 2016 have reduced [7] the false detection of MAs and HEs on the BVs using Frangi filters with lesionness measure. Images were pre-processed (extraction of green channel and its inversion) and passed through proposed filters for extracting features. Features from the patches were combined to get feature vector which was followed by support vector machines (SVM) classifier to predict whether the image had a lesion or not. The areas under receiver operating characteristic were 0.97 and 0.92 for MAs and Has, respectively.

Diyana *et al.* in 2016 have reviewed [8] various methods used for grading assessment of DR. This paper suggested that the BV segmentation and BV tortuosity measurement would be used to know the retinal diseases severity. Dhiravidachelvi and Rajamani in 2015 have proposed [9] approach to detect the DR, types and its severity and the appropriate treatment. Pre-processing was done to remove salt and pepper noise, and the image was enhanced pixel level. Scale-invariant feature transform feature points, histogram value and the connected components using morphological operations were calculated for both the image and the template image to decide whether the input fundus image is normal or abnormal and early or advanced stage. OTSU image segmentation with different thresholds has been applied to extract tiny dots, EXs, and hemorrhages (HEs) based on the numbers and areas of these lesions near macula the severity can be determined.

As the population is growing fastly in nowadays Arenas-Cavalli *et al.* in 2015 have presented [10] a web-based application technique to detect automatically the lesions of DR. Patient's fundus image will be uploaded in the health-care center and in the remote place automated DR screening by means of image processing will be done and the results will be referred by ophthalmologists, and finally results notification will be in the health-care center. Color normalization, contrast enhancement, and noise removal were done. Processing includes feature extraction, optic disc detection using KNN regression, image segmentation using fuzzy c-means (FCM) clustering and morphological operation.

Maher *et al.* in 2015 have detected [11] and classified DR using proposed automated system. Morphological operations were performed to segment the BVs and EXs and to extract features, and they classified the disease stages as normal, NPDR and PDR by using multiclass naive bayes classifier. Pre-processing includes Gaussian filtering and elimination of background variations using shade correction method. In 2015 Shriwas *et al.* have reviewed [12] methods of pre-processing, processing and classification for the detection of lesions and classification of DR. Retinopathy grades are 0 for normal, 1 for (MA 0-5), 2 for (MA 6-14 or HE 1-4 and 0 neovascularisation). 3 for (MA ≥15 or HE ≥5 or NV =1). Messidor, drive and stare are the three major databases used for retinal images.

In 2015, Mustafa *et al.* have reviewed [13] various methods of finding the retina vascular tortuosity for grading assessment of DR. Mookiah *et al.* in 2015 have reviewed various imaging modalities [14] used for diagnosing diabetic macular edema (DME), automated grading systems for DME with fundus images, techniques for detecting and segmenting fovea and EXs. Finally, the authors concluded that fundus imaging is more suitable and affordable for DME grading and telescreening.

Ganesan *et al.* in 2015 have extracted [15] the EXs and the optic disc using K-means, FCM, and principal component analysis (PCA). The comparison was made by taking six image quality parameters and as a conclusion PCA based detection was more efficient than the K-means and FCM. Banerjee in 2015 have designed [16] a decision support system using contextual information to classify retinal abnormalities such as age-related macular degeneration and DR. FCM were used to separate the candidates into three clusters as the diseased retinal image has three different color groups and the matching was done between the candidate segmented image and prototype segmented image along with the contextual information. Accuracy rate was not defined.

In 2015, Bharali *et al*. have proposed image processing methods [17] to detect HEs in fundus images. CLAHE, median and average filtering was done. BV structure was detected by region growing algorithm and eliminated by morphological operations with modified NICK's local threshold algorithm. Deka *et al*. in 2015 developed a novel method [18] for determining the macula and fovea. Accuracy has been calculated as 97.85%. CLAHE was done to improve the image. BV was detected by 5th order discrete wavelet transform (DWT) decomposition followed by morphological opening operation.

Prasad *et al*. in 2015 have classified the images [19] as diabetic or non-diabetic by the use of morphological operations and segmentation techniques for the detection of BVs, EXs and MAs and Haar wavelet transform and PCA were used for the selection of optimal features and the classification was done by the use of back propagation NN (BPNN) and one rule classifiers. The sensitivity, specificity and accuracy for the BPNN classifier were 93.3, 95.23 and 93.8% and for the one rule classifier it was 97.8, 97.5 and 97.75%.

Omar *et al*. in 2014 have segmented EXs [20] in RGB images by applying morphological operations (modified region props function) and a reconstruction technique. This system will be built into a mobile platform to diagnose the DR. RGB to HIS, median filtering and CLAHE was done as the pre-processing.

In 2014, Yin *et al.* have proposed a system [21] able to classify retinal and non-retinal images and performing quality testing of retinal images. This can be used as a pre-processing step to eliminate images with poor quality. Images were represented as Bag of visual words. Structural similarity index and high-level image quality measures have been calculated for determining the likeness between two images and to perform quality testing. The image classification was done by SVM.

Usman Akram *et al.* in 2014 have detected, classified and graded the retinal lesions by the various phases [22]. 16 features were extracted from the morphological operations and Gabor filter banks responses. The following was the work done in this paper: Background separation, extraction of BVs by Gabor wavelet and multilayered threshold, extraction of optic disc by averaging filter, feature extraction, and classification by hybrid classifier (m-Mediods based classifier with a Gaussian mixture model [GMM]). Ramya *et al*. in 2014 have given an idea [23] to detect EXs. Resizing, gray-scale conversion, and filtering were the pre-processing and the BVs and optic disc were extracted by thresholding and circular Hough transform, respectively. Finally, adaptive thresholding was used to detect EXs. Sensitivity and specificity were not defined.

Welikala *et al*. in 2014 have used [24] a novel method for detecting new BVs and to reduce false responses. The two vessel segmentation techniques such as standard line operator and novel modified line operator were applied, and the final decision was performed by combining the outcome of individual SVM classifiers. The disadvantage was that this work would fail when there were new vessels appeared as loops or small networks. Pre-processing includes median filtering to reduce salt and pepper noise, local contrast enhancement and shade correction.

In 2013, Tavakoli *et al*. developed unconventional algorithm [25] to detect and mask optic nerve head and BVs. Fluorescein angiography fundus images were used to detect microaneurysms. BVs were detected by applying Radon transform (RT) with multi-overlapping windows and the microaneurysms were detected by RT and thresholding at the finest level. Contrast stretching and average filtering were done before processing.

Youssef and Solouma in 2012 have applied [26] robust algorithm for determining BVs and EXs in fundus images using image processing algorithms. It can be fully automatic or semi-automatic. Pre-processing includes median filtering and contrast enhancement by top hat morphological operations. The workflow was the extraction of optic disc by Hough transform and canny edge detection, detection of contours in retinal images by simplified snakes contour edge detection algorithm, extraction of BV-tree by morphological closing with two structuring elements and morphological reconstruction algorithm was used to get the final estimate of EXs. Saleh and Eswaran in 2012 have proposed an automated decision support [27] user-friendly system for identifying DR and its severity with respect to location and number of microaneurysms and HAs. Preprocessing includes median filtering and green channel extraction. Processing includes removal of optic disc by centroid distance method, removal of image background, dark spot segmentation by h-maxima transformation and thresholding and feature extraction.

In 2012, Selvathi *et al.* have segmented BVs, EXs, and MAs [28] to classify images using SVM as normal or DR images by performing discrete curvelet transform of the green channel image, morphological operations, texture analysis (GLCM), feature extraction, and classification. Köse *et al.* in 2012 have introduced an algorithm [29] with background image and inverse segmentation for segmenting DR lesions (hard EXs, cotton wool spots, MAs, and HEs) to measure changes across the whole retina. A comparison was done between Bayesian, manual method and region growing segmentation method. In 2012, Patil and Chaudhari proposed tool for enhancing retinal image to detect DR lesions [30]. Image enhancement method (rotated versions of Kirsch masks, I and IInd derivative and contrast stretching transformation) was used to adjust image properties such as mean intensity, contrast, and sharpness with respect to the intensity of pixels and this processed image can be used as input for automated image processing techniques. Image was sharpened using spatial filters.

Saleh and Eswaran in 2012 have provided an automated DR diagnosis system [27] with a user-friendly interface. This paper discussed the methods (h-maxima transformation followed by thresholding and feature extraction) used for the extraction and classification of MAs and HEs. The number and location of MAs and HEs was used to identify disease severity. Pre-processing includes green channel extraction, background normalization, and optic disc removal. Winder *et al*. in 2009 had reviewed over a 10-year period papers for [31] algorithms used for pre-processing, detection and segmentation of optic disc, BV segmentation, macula and fovea localization and detection and retinopathy segmentation. It was concluded to identify the area where the research is to be improved.

In 2009, Sánchez *et al*. have applied mixture models and dynamic thresholding [32] for the detection of EXs. Optic disc was removed and edges are enhanced by Kirsch's method. The authors have left spatial correlation at neighboring pixels. Luminosity and contrast enhancement was done using mean and standard deviation of pixels. Sopharak *et al.* in 2008 have detected hard EXs [33] on low-contrast images using morphological and Otsu thresholding in the non-dilated and low contrast fundus images. Pre-processing includes RGB to HIS conversion, median filtering, CLAHE and bi-linear interpolation. Distance between the macula and the EXs were also determined to help the ophthalmologists to know the severity of the disease. Structuring element of disc shaped with fixed radius was used. Distinguishing hard and soft EXs will be the future work. Akila and Kavitha in 2014 [34] have detected the hard EXs by FCM and K means clustering and classified by random forest classifier. The accuracy achieved was 92.94%.

ALGORITHMS USED FOR PRE-PROCESSING

Local contrast enhancement (CLAHE), correction of non-uniform illumination, color normalization, noise removal, histogram analysis, median filtering, shade correction, conversion to his color space, Gaussian filtering, adaptive contrast enhancement, mathematical model, image filtering techniques, and green channel extraction.

ALGORITHMS USED FOR DETECTION AND SEGMENTATION OF OPTIC DISC

Active contour models, principle component analysis algorithm, snakes algorithm watershed transform, point of convergence of BVs, extraction of high intensity pixels, point distribution model, extraction of maximum contrast pixels, adaptive thresholding, morphological operations, KNN regressor, Hough transform and canny edge detection, performing an and operation with mask image to remove circular border, centroid distance method, multilevel wavelet decomposition and recursive region growing, modified sobel operator, saliency-based optic disc segmentation, Haar DWT-based pyramidal decomposition, Hausdorff distance method template matching, line operator, fuzzy convergence, KNN location regression, circular transformation and super pixel classification.

ALGORITHMS/METHODS USED FOR DETECTION AND SEGMENTATION OF BVS

Vessel tracking algorithm, matched filter, morphological analysis, PCA, wavelet and edge detection, steerable/Gaussian filters, watershed transform and thresholding, classification by NN, standard line operator and modified line operator, segmentation based on pixel's feature vector, morphological closing with two structuring elements, kirsch operator, discrete curvelet transform of green channel of the image, histogram analysis, RT and multi overlapping windows, template matching and contour reconstruction, multiscale Hessian Eigen value analysis to enhance vessels, GMM and expectation maximization clustering to classify vessels, least square SVM to classify veins based on four colour features and extraction of four features (mean angle change, FFT, vessels length upon distance, Arc to chord ratio) to measure tortuosity.

METHODS USED FOR THE LOCALIZATION OF FOVEA AND MACULA

Method of searching for low pixel areas near the optic disc, the darkest area which is 2.5 times the diameter of the optic disc will be considered as a macula, By fitting a parabola on the main vessels having its vertex at the OD centre, by determining a line that was roughly passing through the OD and the macula using a parabolic model of the vasculature and localize the fovea by its distance from the OD, location of the fovea as the region of minimum vessel density within a search region, matching correlation, Mathematical morphology active contour model, active shape model and geometrical relation, BPF, region growing and geometric relation, singular value decomposition, point distribution model, Markov random fields, and adaptive thresholding.

ALGORITHMS USED FOR THE DETECTION OF LESIONS

Region growing, classification algorithms, adaptive intensity thresholding with a "moat operator, Otsu image segmentation, morphological analysis, segmentation using FCM clustering and classification by NN classifier, simplified snakes contour edge detection algorithm, morphological reconstruction algorithm, recursive region growing, h-maxima transformation and thresholding to extract MAs and Has, Kirsch's edges for EXs detection, three stage intensity transformation and detection of white lesions from multilevel histogram analysis, Histogram modeling using mixture model and dynamic thresholding, adaptive region growing method followed by background correction and inverse segmentation method, RT and fine level of thresholding. local variance, size, and the local contrast were used to segment the EX regions, EXs segmentation using K-means clustering, Prewitt operators and Otsu thresholding, Color and Fishers linear discriminant analysis, FCM clustering, Kirsch's operator and Riesz transform, amplitude modulation frequency modulation, circular Hough transformation and multi-scale correlation filtering and dynamic thresholding to extract MAs, OD thresholding by Nilblack's method and the regionprops function and OD detection by FIR LPF, Frangi filters and Gabor filters to extract features. BV detection and elimination by applying region growing algorithm, 5th order DWT decomposition, morphological operations and local threshold modified NICK's algorithm.

NN AND FUZZY LOGIC

Another approach to detect lesions in DR was also suggested by the authors. The following are the summary of papers used NN and fuzzy logic.

Rahim *et al*. in 2016 have d esigned automated system [35] for determining maculopathy and DR by employing fuzzy image

Table 1: Comparison of results in the image processing

Paper	Number of images taken	Databases	Sensitivity (%)	Specificity (%)	Accuracy/execution time
Kumar *et al.* [1]	1344	Regional institute of ophthalmology	80	50	-
Liu *et al.* [2]	76	DiaRetDB1, e-ophtha EX dataset	DiaRetDB1: 83	75	79
Kumar *et al.* [3]	130	DIARETDB1, DRIVE, STARE and live images from the eye foundation hospital, Coimbatore.	-	-	96.9
Wu *et al.* [5]	248	ROC and e-optha	-	-	-
Bharkad [6]	369	DRIVE, DIRATEDB0, DIRATEDB1 and DRIONS	74.60-87.07	99.39-99.61	96.92-100 27.55 seconds
Srivastava *et al.* [7]	143	DIARETDB1 and MESSIDOR	-	-	-
Dhiravidachelvi and Rajamani [9]	100	RR eye research institute, Chennai	-	-	93
Arenas-Cavalli *et al.* [10]	275	CRS	91.9	65.2	9.6 minutes
Maher *et al.* [11]	130 89	DIARETDB0, DIARETDB1	85	97.3	89.6
Ganesan *et al.* [15]	-	-	95.2795	99.804	98.9625
Bharali *et al.* [17]	1914	HRF, DIARETDB0, DIARETDB1, MESSIDOR and local databases	97.3	98.92	98.22
Deka *et al.* [18]	1020	DRIVE, MESSIDOR, DIARETDB1, HRF, STARE	-	-	97.85
Omar *et al.* [20]	89	DIAREDB1	85.39	-	-
Yin *et al.* [21]	35342	SMES, SCES and BMES	-	-	99.54
Usman Akram et al. [22]	1410	DRIVE, STARE, DIARETDB, and MESSIDOR	MAs and HA: 97.83 EXs: 97.39	98.36 98.02	98.12 97.56
Welikala *et al.* [24]	60	MESSIDOR, St Thomas' Hospital	86.2	94.4	450 seconds
Tavakoli *et al.* [25]	192	Mashhad database local database from Tehran and retinopathy online challenge	81	93	-
Youssef and Solouma [26]	100	NILES, STARE	80	100	-
Saleh and Eswaran [27]	98	University Malaya Medical Centre (UMMC)	MAs: 84.31 HEs: 87.53 DR: 89.47	93.63 95.08 95.65	-
Selvathi *et al.* [28]	40 89 1200	DRIVE, DIARETDB1 AND MESSIDOR	-	-	93
Köse *et al.* [29]	328	Karadeniz Technical University	HEs: 98.1 CWS: 97.6 MAs: 95.1 HEM: 93.2	99.8 99.6 99.3 98.3	<15 seconds
Saleh and Eswaran [27]	98	University Malaya Medical Centre (UMMC)	MAs: 84.31 HAs: 87.5	93.63 95.08	-
Sánchez *et al.* [32]	80	Instituto de of talmobiología Aplicada at University of Valladolid, Spain	100	90	-
Sopharak *et al.* [33]	60	Thammasat University Hospital	80	99.5	3 minutes
Akila and Kavitha [34]	-	-	88.8	94	92.94

preprocessing, morphological processing for retinal structures localization and EXs detection, and for classification six features were extracted (three for EXs and another three for macula). The classifiers were k-nearest neighbor, radial basis function (RBF) Kernel SVM, polynomial Kernel SVM, and Naïve-Bayes. Results with good accuracy were achieved by KNN and RBF Kernel SVM classifiers.

Pratt *et al.* in 2016 have discussed first the five class classification of DR [36] using convolutional NN. The classes were normal, mild DR, moderate DR, severe DR, and proliferative DR. The trained network can classify thousands of images every minute and hence to be used in real-time. It achieved 95% specificity, 75% accuracy, and 30% sensitivity. Color normalization and image resizing were the pre-processing steps.

Mahendran *et al.* in 2015 have detected and localized the EXs [37] by applying segmentation technique (neighborhood based). SVM and PNN classifiers were used to get the disease severity. The compared results showed accuracy for classification that was 97.89% for state vector machine classifier and 94.76% for PNN classifier. Divya in 2015 has proposed algorithm [38] for determining features such as BVs, EXs, MAs, and OD. Based on that she identified the severity of DR, Kirsch algorithm used for detecting BVs, Fuzzy clustering algorithm for extracting EXs and morphological distance-based algorithm for the detection of MAs.

Franklin and Rajan have segmented retinal BVs [39] for identifying vessel size by employing multilayer perceptron NN. The vascular structure helps to classify the severity of DR. The weights in a feed-forward network was changed by employing back propagation algorithm. The measured accuracy was 95.03%. Thomas and Mahesh [40] have detected EXs using morphological operations and classified as normal, weak and hard EXs by fuzzy logic. Non-overlapping MFs produced inaccurate results and the work needed to be improved to detect EXs pixels having very low-intensity values.

Akram *et al.* [41] have developed the system with three stages for the early finding of MAs. A bank of Gabor filters was employed to extract the candidates, formation of 15 feature vectors and classification of candidates as MAs or non-microaneurysms was achieved using hybrid classifier which was GMM classifier, state vector machine classifier, and multimodal Mediod based modeling approach classifier. The sensitivity of 98.64%, specificity of 99.69%, and accuracy of 99.40% was achieved. Basha *et al*. in 2013 have presented a method for detecting new vessels [42] on the optic disc. Vessels like regions were extracted using green component of the RGB image, and the new vessel segments were detected using morphological watershed transform. From these candidate regions, 15 features were extracted for each segment. By using these features and SVM classifier each segment was classified as normal or abnormal vessels. Accuracy was not defined.

Hassan *et al*. in 2012 have identified and detected new BVs from the normal BVs [43]. Window based classification was done based on number of BVs and the area involved. The specificity of 89.4% and sensitivity of 63.9% was achieved. Sanchez *et al*. have proposed [44] a new method for detecting hard EXs based on six high-level contextual features rather than local-based features in the computer-aided diagnosis (CAD) system. The green channel output was convolved with 14 digital filters, and then KNN classifier was used to classify the pixels. Obtaining probability of each pixel and threshold them to get bright lesion candidate clusters. There was local and contextual classification by linear discriminant classifier. Contextual features were extracted from the posterior probabilities, and the most discriminative feature selection was done by sequential forward floating selection. Figure of Merit of 0.945 was achieved with this CAD system.

García *et al*. in 2010 have used four NN classifiers [45] such as multilayer perceptron, state vector machine, RBF, and their combination with voting majority technique to detect one of the red lesions. Color and shape of 29 features were extracted. Best performance and low complexity were achieved with RBF. Mean sensitivity and mean positive predictive value for lesion classification was 86.01% and 51.99%, respectively. Mean specificity, mean sensitivity, and mean accuracy for image level classification was 56.00%, 100% & 83.08%, respectively.

In 2009, García *et al.* have used morphological operations to detect hard EXs [46] and 18 features were extracted and classified by three NN classifiers (multilayer perceptron, state vector machine, and RBF). Authors specified the values of mean specificity, mean sensitivity, and mean accuracy for all the three classifiers. Basha and Prasad in 2008 have combined [47] IP and fuzzy logic to detect DR and its lesions. The fundus image was segmented by morphological operations to find out the hard EXs, soft EXs, MAs, and hemorrhages. Five different color space values for those abnormal regions were calculated to form fuzzy sets, and the average of five outputs was determined. The result is positive if the average is 1. Negative if the average is 0 and the other intermediate outputs denote the percentage of disease severity.

As the Genistein protects eye from retinal inflammation, Dongare *et al.* in 2015 investigated [48] how the Genistein reacted for glucose toxicity and protects retinal pigment epithelium cells. Results showed that it was the vigorous treating agent for diabetic-related diseases. In 2015, Aly [49] has found the useful effects of oats on the DR. The changes in the retina were noted by the application of Fourier transform infrared spectroscopy. The final suggestion was the requirement of optimization for dosing and commercial preparation of the medicine.

RESULTS AND DISCUSSION

A comparison of performances has been made in Table 1 to identify where the research is to be improved. Many research papers have come up with different algorithms but acceptable levels of sensitivity and specificity have not yet been reached, and only less work has been reported for the detection of fovea and macula.

CONCLUSION

This review paper analyzed the various steps and different algorithms used recently for the detection and classification of DR lesions. Algorithms used for pre-processing, processing, segmenting anatomical structures, and detection of lesions were also included. Performances were evaluated in terms of sensitivity, specificity, area under the curve and accuracy. Different databases and the number of images taken for training and testing were also mentioned. Suggestions, future work and the area to be improved were also analyzed.

REFERENCES

1. Kumar PN, Deepaka RU, Sathar A, Sahasranamam V, Kumar RR. Automated detection system for diabetic retinopathy using two field fundus photography. Procedia Comput Sci 2016;93:486-94.
2. Liu Q, Zou B, Chen J, Ke W, Yue K, Chen Z, *et al*. A location-to-segmentation strategy for automatic exudates segmentation in colour retinal fundus images. Comput Med Imaging Graph 2016;55:78-86.
3. Kumar HS, Bharathi PT, Madhuri R. A novel method for image analysis and exudates detection in retinal images. Int J Adv Res Innov 2016;4(1):219-23.
4. Besenczi R, Tóth J, Hajdu A. A review on automatic analysis techniques for color fundus photographs. Comput Struct Biotechnol J 2016;14:371-84.
5. Wu B, Zhu W, Shi F, Zhu S, Chen X. Automatic detection of microaneurysms in retinal fundus images. Comput Med Imaging Graph 2016;55:106-12.
6. Bharkad S. Automatic segmentation of optic disk in retinal images. Biomed Signal Process Control 2016;31:483-98.
7. Srivastava R, Duan L, Wong DW, Liu J, Wong TY. Detecting retinal microaneurysms and hemorrhages with robustness to the presence of blood vessels. Comput Methods Programs Biomed 2017;138:83-91.
8. Diyana M, Zulkifleya MA, Hussain A, Halim HW, Mustafa NB, Ting LS. Diabetic retinopathy assessment: Towards an automated system. Biomed Signal Process Control 2016;24:72-82.
9. Dhiravidachelvi E, Rajamani V. A novel approach for diagnosing diabetic retinopathy in fundus Images. J Comput Sci 2015;11(1):262-8.
10. Arenas-Cavalli JT, Rios SA, Pola M, Donoso R. A web-based platform for automated diabetic retinopathy screening. Procedia Comput Sci 2015;60:557-63.
11. Maher RS, Panchal D, Kayte J. Automatic diagnosis microaneurysm using fundus images. Int J Adv Res Comput Sci Softw Eng 2015;5(10):126-30.
12. Shriwas RS. Retinal image processing for diabetic retinopathy. Int J Eng Sci Res Technol 2015;594-598.ISSN:2277-9655.
13. Mustafa NB, Wan Zaki WM, Hussain A. A Review on the Diabetic Retinopathy Assessment Based on Retinal Vascular Tortuosity; 2015.
14. Mookiah MR, Acharya UR, Fujita H, Tan JH, Chua CK, Bhandary SV, *et al.* Application of different imaging modalities for diagnosis of Diabetic Macular Edema: A review. Comput Biol Med 2015;66:295-315.
15. Ganesan P, Chelladurai R, Sureshkumar M, Kalist V. Automatic identification and segmentation of exudates and optic disc in colour fundus images of the diabetic retinopathy human retina. Res J Pharm Biol Chem Sci 2015;6(4):908-15.
16. Banerjee S. Case based reasoning in the detection of retinal abnormalities using decision trees. Procedia Comput Sci 2015;46:402-8.
17. Bharali P, Medhi JP, Nirmala SR. Detection of Hemorrhages in Diabetic Retinopathy Analysis using Color Fundus Images; 2015.
18. Deka D, Medhi JP, Nirmala SR. Detection of Macula and Fovea for Disease Analysis in Color Fundus Images; 2015.
19. Prasad DK, Vibha L, Venugopal KR. Early Detection of Diabetic Retinopathy from Digital Retinal Fundus Images; 2015.
20. Omar M, Hossain A, Zhang L, Shum H. An Intelligent Mobile-based Automatic Diagnostic System to Identify Retinal Diseases using Mathematical Morphological Operations; 2014.
21. Yin F, Wong DW, Yow AP, Lee BH, Quan Y, Zhang Z, *et al.* Automatic retinal interest evaluation system (ARIES). Conf Proc IEEE Eng Med Biol Soc 2014;2014:162-5.
22. Usman Akram M, Khalid S, Tariq A, Khan SA, Azam F. Detection and classification of retinal lesions for grading of diabetic retinopathy. Comput Biol Med 2014;45:161-71.
23. Ramya J, Soundarya S, Nagoormeeral A, Revathi E. Detection of exudates in color fundus image. Int J Innov Res Sci Eng Technol 2014;3(3):10659-65.
24. Welikala RA, Dehmeshki J, Hoppe A, Tah V, Mann S, Williamson TH, *et al*. Automated detection of proliferative diabetic retinopathy using a modified line operator and dual classification. Comput Methods Programs Biomed 2014;114(3):247-61.
25. Tavakoli M, Shahri RP, Pourreza H, Mehdizadeh A, Banaee T,

Toosi MH. A complementary method for automated detection of microaneurysms in fluorescein angiography fundus images to assess diabetic retinopathy. Pattern Recognit 2013;46(10):2740-53.
26. Youssef D, Solouma NH. Accurate detection of blood vessels improves the detection of exudates in color fundus images. Comput Methods Programs Biomed 2012;108(3):1052-61.
27. Saleh MD, Eswaran C. An automated decision-support system for non-proliferative diabetic retinopathy disease based on MAs and HAs detection. Comput Methods Programs Biomed 2012;108(1):186-96.
28. Selvathi D, Prakash NB, Balagopal N. Automated detection of diabetic retinopathy for early diagnosis using feature extraction and support vector machine. Int J Emerg Technol Adv Eng 2012;2(11):103-8.
29. Köse C, Sevik U, Ikibas C, Erdöl H. Simple methods for segmentation and measurement of diabetic retinopathy lesions in retinal fundus images. Comput Methods Programs Biomed 2012;107(2):274-93.
30. Patil JD, Chaudhari AL. Tool for the detection of diabetic retinopathy using image enhancement method in DIP. Int J Appl Inf Syst IJAIS 2012;3(3):54-6.
31. Winder RJ, Morrow PJ, McRitchie IN, Bailie JR, Hart PM. Algorithms for digital image processing in diabetic retinopathy. Comput Med Imaging Graph 2009;33(8):608-22.
32. Sánchez CI, García M, Mayo A, López MI, Hornero R. Retinal image analysis based on mixture models to detect hard exudates. Med Image Anal 2009;13(4):650-8.
33. Sopharak A, Uyyanonvara B, Barman S, Williamson TH. Automatic detection of diabetic retinopathy exudates from non-dilated retinal images using mathematical morphology methods. Comput Med Imaging Graph 2008;32(8):720-7.
34. Akila T, Kavitha G. Detection and classification of hard exudates in human retinal fundus images using clustering and random forest methods. Int J Emerg Technol Adv Eng 2014;4(2):24-9.
35. Rahim SS, Palade V, Shuttleworth J, Jayne C. Automatic screening and classification of diabetic retinopathy and maculopathy using fuzzy image processing. Brain Inform 2016;3(4):249-67.
36. Pratt H, Coenen F, Broadbent DM, Harding SP, Zheng Y. Convolutional neural networks for diabetic retinopathy. Procedia Comput Sci 2016;90:200-5.
37. Mahendran G, Dhanasekaran R. Investigation of the severity level of diabetic retinopathy using supervised classifier algorithms. Comput Electr Eng 2015;45:312-23.
38. Divya SN. Detection of diabetic retinopathy using kirsch edge detection and watershed transformation algorithm. Int J Adv Res Ideas Innov Technol 2015;1(4):1-7.
39. Franklin SW, Rajan SE. Computerized screening of diabetic retinopathy employing blood vessel segmentation in retinal images. Biocybern Biomed Eng 2014;34(2):117-24.
40. Thomas N, Mahesh TY. Detection and classification of exudates in diabetic retinopathy. Int J Adv Res Comput Sci Manag Stud 2014;2(9):296-305.
41. Akram MU, Khalid S, Khan SA. Identification and classification of microaneurysms for early detection of diabetic retinopathy. Pattern Recognit 2013;46:107-16.
42. Basha AH, Udhayakumar S, Sujatha E. Detection of visual impairments using back propagation neural networks. Int J Comput Sci Eng Technol 2013;4(3):274-8.
43. Hassan SS, Bong DB, Premsenthil M. Detection of neovascularization in diabetic retinopathy. J Digit Imaging 2012;25(3):437-44.
44. Sanchez CI, Niemeijer M, Schulten MS, Abramoff M, van Ginneken B. Improving Hard Exudate Detection in Retinal Images Through a Combination of Local and Contextual Information; 2010.
45. García M, López MI, Alvarez D, Hornero R. Assessment of four neural network based classifiers to automatically detect red lesions in retinal images. Med Eng Phys 2010;32(10):1085-93.
46. García M, Sánchez CI, López MI, Abásolo D, Hornero R. Neural network based detection of hard exudates in retinal images. Comput Methods Programs Biomed 2009;93(1):9-19.
47. Basha SS, Prasad KS. Automatic detection of hard exudates in diabetic retinopathy using morphological segmentation and fuzzy logic. Int J Comput Sci Netw Secur 2008;8(12):211-8.
48. Dongare S, Rajendran S, Senthilkumari S, Gupta SK, Mathur R, Saxena R, *et al*. Genistein alleviates high glucose induced toxicity and angiogenesis in cultured human RPE cells. Int J Pharm Pharm Sci 2015;7(8):294-8.
49. Aly EM. FTIR analysis for retina associated with diabetic changes and treatment with oat. Int J Pharm Pharm Sci 2015;7(10):277-80.