Automatic Detection and Classification of Malarial Retinopathy-Associated Retinal Whitening in Digital Retinal Images

MUHAMMAD USMAN AKRAM*, ABU BAKAR NISAR ALVI*, AND SHOAB AHMED KHAN*

RECEIVED ON 06.08.2016 ACCEPTED ON 21.02.2017

ABSTRACT

Malarial retinopathy addresses diseases that are characterized by abnormalities in retinal fundus imaging. Macular whitening is one of the distinct signs of cerebral malaria but has hardly been explored as a critical bio-marker. The paper proposes a computerized detection and classification method for malarial retinopathy using retinal whitening as a bio-marker. The paper combines various statistical and color based features to form a sound feature set for accurate detection of retinal whitening. All features are extracted at image level and feature selection is performed to detect most discriminate features. A new method for macula location is also presented. The detected macula location is further used for grading of whitening as macular or peripheral whitening. Support vector machine along with radial basis function is used for classification of normal and malarial retinopathy patients. The evaluation is performed using a locally gathered dataset from malarial patients and it achieves an accuracy of 95% for detection of retinal whitening and 100% accuracy for grading of retinal whitening as macular or non-macular. One of the major contributions of proposed method is grading of retinal whitening into macular or peripheral whitening.

Key Words: Malarial Retinopathy, Retinal Whitening, Macular Whitening, Cerebral Malaria.

1. **INTRODUCTION**

alarial Retinopathy is often characterised by Retinal whitening, vessel discoloration, Papilledema and retinal haemorrhages in digital retinal images. Out of these abnormalities, retinal whitening and vessel discoloration are associated with cerebral malaria. Early detection of these retinal abnormalities can lead to the detection of cerebral malaria. Cerebral Malaria remains the biggest killer amongst all forms of parasitic malaria, especially in tropical and equatorial regions of the globe [1]. Retinal whitening is characterised as macular whitening or peripheral

whitening. In cases of macular whitening, the fovea and macular region is affected by a patchy pacification. In cases of peripheral whitening, the periphery of the macular region especially the areas along the blood vessels are affected. Retinal whitening in fundus images is one of the most distinct signs of cerebral malaria [1]. Unlike vascular haemorrhages and Papilledema, retinal whitening manifests itself as a unique sign of cerebral malaria. Early diagnosis and prognosis can be done through an automated detection and classification system and can be very effective in areas where occurrence

Corresponding Author (E-Mail: usmakram@gmail.com) National University of Sciences & Technology, Islamabad.

Mehran University Research Journal of Engineering & Technology, Volume 36, No. 4, October, 2017 [p-ISSN: 0254-7821, e-ISSN: 2413-7219]

of the disease is common and can be fatal. Fig. 1 shows magnified regions of fundus image of the retina with macular and peripheral whitening clearly seen in the area around the macula and blood vessels respectively.

Automatic detection and classification of diseases through computer based methods involves development of clinical decision support methods that can act as surrogates in areas where specialist medical opinion is not available. The methods involve extraction of highly discriminative features from sample image datasets of healthy and non-healthy subjects. These features are extracted using image processing and statistical methods in an image and are used for classification through supervised learning methods associated with machine learning.

Various medical decision support systems [2,3] have been developed that assist the specialists in diagnosis, prognosis and treatment of various ailments. The fundus images of normal subjects and subjects with disease are used to develop a machine learning system that assists in the decision making process. In case of retinal region, the region is manifested by abnormalities like exudates, MA (Microaneurysms), hemorrhages, colored spots, discoloration and whitening. Although the features extracted for all these abnormalities are different, however, the underlying image processing techniques have similarities that can be exploited in detection of these abnormalities.

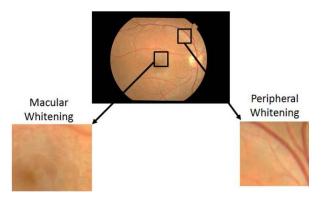


FIG.1. FUNDUS IMAGE SHOWING MAGNIFIED REGIONS OF MACULAR AND PERIPHERAL WHITENING

Automatic detection and classification of various diseases through analysis of fundus images has interested researchers for many years [4]. Researchers have used the knowledge base developed in various ophthalmological studies for developing computer based statistical models to diagnose various ailments. Most of this research focuses on the development of image processing techniques to detect the abnormalities in the retinal region and then extract discriminatory features from these areas using preprocessing, noise removal, image enhancement and segmentation.

The paper is organized as follows. Section 2 highlights the related work with respect to malarial retinopathy, cerebral malaria and other ophthalmological disorders. Section 3 discusses the proposed methodology of the system. Section 4 highlights the experimental results of the system supported by various analytical and statistical parameters. Finally, Section 5 concludes the paper briefly.

2. RELATED WORK

Automatic detection of malarial retinopathy is vital for treatment of patients suffering from cerebral malaria. Most of the researchers have developed computerized methods and models for this purpose using fundus images. Retinal whitening is a very distinct sign for cerebral malaria and has been discussed in literature [1] for clinical diagnosis of the disease. However, retinal whitening has not been used in any of these models as a detection and classification parameter. There are some methods discussed in literature that detect malarial retinopathy using other biomarkers. The focus of research has been the detection of abnormalities and extracting features from these areas.

Splats are segments in images that have similar color and spatial location. Splats can be used to extract various color and statistical features that are useful for classification [5,6]. Selection of appropriate and discriminatory features from these splats is very important to obtain high classification

results. Joshi et. al. [7] proposed an automated system for detection of malarial retinopathy associated hemorrhages. The system used over 200 fundus images to develop a pattern recognition system that classified the hemorrhages associated with malarial retinopathy. The system achieved a sensitivity of 84.4% and specificity of 96.6% for detection of hemorrhages using various splat and legion based features. Tang et. al. [8] proposed a splat feature classification based scheme that extracts features from various regions which are used for classification of hemorrhages. The system was able to achieve an area under the receiver operating curve value of 0.96 at splat level and 0.87 at image level respectively.

Other than these articles, no such method exists which directly deals with malarial retinopathy. However there are a number ofmethods for hemorrhage detection due to other retinal diseases such as diabetic retinopathy. In studies of automated systems for diagnosis of abnormalities, HMA (Hemorrhage and Microaneurysm) are also considered. A moat operator was used for automated detection of HMA [9] using only 30 retinal images. A similar study was conducted by Hatanaka et. al. [10] on hemorrhage detection using 125 digital retinal images. HSV (Hue, Saturation and Value) color space and Mahalanobis distances were used for classification. A similar computer aided system for classification was proposed in [11]. They were able to obtain accuracies of around 83% using the proposed methods.

In fundus images, the localization of optical disk and macula is an important step before further analysis on detection of abnormalities can be done. Similarly, enhancement and segmentation of blood vessels in fundus images is important to localize the areas affected by any retinal abnormalities. Geometric relationship between the optical disk and the blood vessels was used by Hoover et. al. [12] to determine the location of optical disk. Similarly, morphological operations like opening, closing, dilation and erosion along with water transformation have been used by Walter et. al. [13] to localize the optical disk in fundus images.

Classification methods are important in supervised machine learning algorithms. Various parameters for accuracy and similar other measures are computed for assessment of system performance. Multiple supervised learning and classification methods [14] have been used by researchers for this purpose. SVM (Support Vector Machines) and FCM (Fuzzy C-Mean) classification were usedby Sopharaket et. al. [15] for classification using a feature set comprising edge pixel location, cluster size and cluster intensity. A multi-layer NN (Neural Network) was used by Osareh et. al. [16] comprising various color and statistical features for classification of exudates in fundus images. Yazid et. al. [17] proposed another FCM based classification method for detection of exudates and optical disk in fundus images. Yasmeen et. al. [18] proposed a method for localization and detection of optical disk and compared the classification results with other similar models. The system achieved optical diskclassification accuracy of around 95% on public dataset images. A similar statistical classification method based on brightness adjustment procedure was used by Wang et. al. [19] to classify exudates in fundus images. Wavelet transform and supervised density-based classifier was used for MAclassification by Quellec et. al. [20]. The technique was evaluated on 120 images for the classification of MAs.

It is clear from the literature that there are very few articles on automated detection of malarial retinopathy and their scope is limited to haemorrhage detection only. There is no significant work which has been carried out on detection of retinal whitening. However, there are some clinical studies to report different signs of MR and also to highlight the significance of retinal whitening [5-8]. The paper proposes a medical decision support system to automatically detect and classify the retinal whitening and its types using fundus images. The system also distinguishes the normal subjects from the non-healthy subjects. This is the main contribution of this article as it is a unique study carrying an automated system for detection of retinal whitening.

3. PROPOSED METHODOLOGY

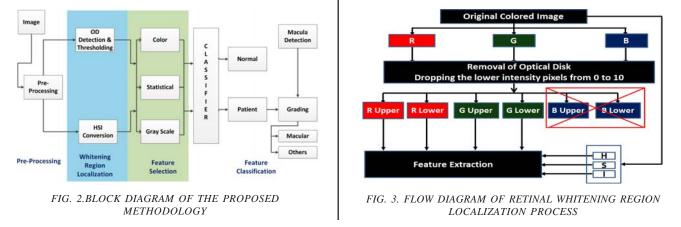
Automatic detection of malarial whitening in fundus images can be vital for early treatment of patients. Decision support systems can be live-savers in remote locations where specialist care is not available for patients. In this article, we propose an automatic detection and classification system that detects and classifies the malarial retinopathy associated retinal whitening. The proposed system consists of stages for pre-processing, retinal whitening region localization, feature extraction, feature selection and classification. The proposed system uses concepts of image processing to select discriminant features from the image dataset. These features are then used to train the classifier and subsequently the training model is used to classify the test data as normal or subjects with retinal whitening. The system also localizes macula which is then used to further grade the retinal whitening subjects as subjects with macular whitening or other forms of whitening, mostly peripheral whitening. Fig. 2 shows the block diagram of the proposed methodology.

3.1 Pre-Processing

The first step of pre-processing involves basic processing on the raw data before complex processing steps are adopted on the images dataset. Some of the acquired images in the dataset correspond to a different resolution, so in the pre-processing step the images in the dataset are re-sized to a resolution of 1536x2048 for uniformity in all the corresponding steps.

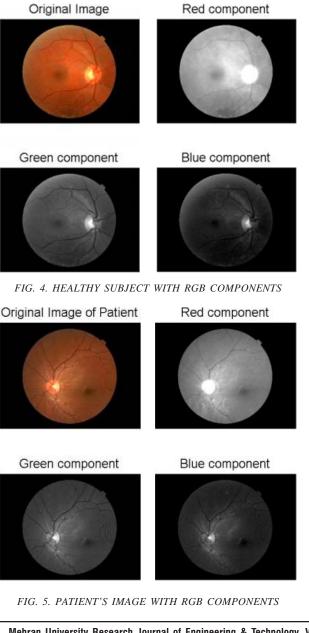
3.2 Retinal Whitening Region Localization

Once all the images in the dataset have a uniform resolution, the next step is the localization of regions containing retinal whitening in the fundus images. To highlight the areas of retinal whitening, pixels corresponding to the optical disk must be removed for a clear visualization of the image. For this purpose, first the optical disk is removed from the image as the high intensity value pixels corresponding to the optical disk have no role in the localization of whitening regions. The proposed algorithm uses intensity based segmentation for extraction of optic disc [21]. The boundary of OD (Optical Disk) is extracted by ellipse fitting. Once the pixels corresponding to the optical disk have been removed from the image, then a mean-based thresholding approach is used to segregate the image into two portions. Subsequent feature extraction is done on these two portions of the image. Fig. 3 shows the complete flow of this process. Fig. 4 shows the colored image of a healthy subject and corresponding RGB (Red, Green, Blue) components. Fig. 5 shows the colored image of a patient's retina and the corresponding RGB components.



Mehran University Research Journal of Engineering & Technology, Volume 36, No. 4, October, 2017 [p-ISSN: 0254-7821, e-ISSN: 2413-7219] 944

It can be seen in the corresponding images that the red and green components of both images have some contrast information, but the contrast information of blue component is not meaningful. So the blue component is dropped for all corresponding computations. Fig. 6 shows the colored image of a healthy subject and the histogram of RGB components. Figs.7-8 shows the colored image of a patient's image and the histogram of RGB components.



Detection of Optical Disk: Most of the high intensity pixel values in the fundus images are associated with the OD. The removal of these pixels from the image helps in the segregation of retinal whitening pixels in the image. The process for detection of OD is explained in [9] and the same method has been used. High intensity pixels associated with OD are removed from the image using a 80x80 window. After the removal of these pixels, mean based thresholding is performed on the image and multiple features are computed from the image. Fig. 9 shows the colored image and the RGB components of a normal subject after OD removal. Fig. 10 shows the colored image and the histogram of the RGB components of a normal subject after OD removal. Fig. 11 shows the colored image and the corresponding RGB components of a patient's image after OD removal and Fig. 12 shows the colored image and the corresponding histogram of a patient's image after OD removal.

It can be seen that the high intensity pixels due to the OD are removed and the histogram points to a clear change in the image mean intensity and the histogram peak is shifted towards pixels of a lesser intensity than the images in which OD pixels were present.OD region is saturated in red plane and by removing OD pixels reduces the count of intesities from 250-255 in red plane.

Mean-Based Thresholding: In this method, following steps are taken for the localization of white regions in the image after OD removal.

It can be seen that most fundus images have an outer layer of low intensity (black) pixels, which are not required in any meaningful processing. From each component, the intensity values between 0-10 are dropped. After dropping these values, the mean intensity value of each colored component is computed. So we have mean intensity valuesfor RGB components of the image. Also, no significant change can be seen in the histogram for the blue component because the contrast is low.

Based on the mean intensity value for all components, each RGB component image is sub-divided into 2 parts. Various features are computed from these regions for the red and green component. The pixel values above the mean correspond to the upper region and the pixel value below the mean to the lower region respectively. The details of these features is explained in the next section.

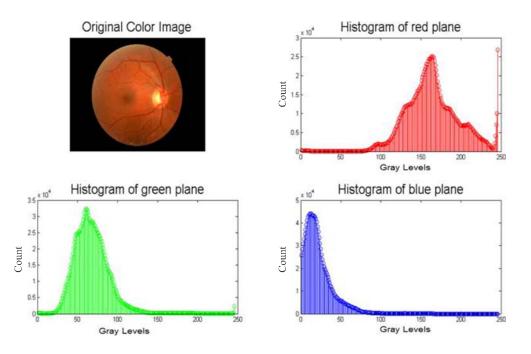
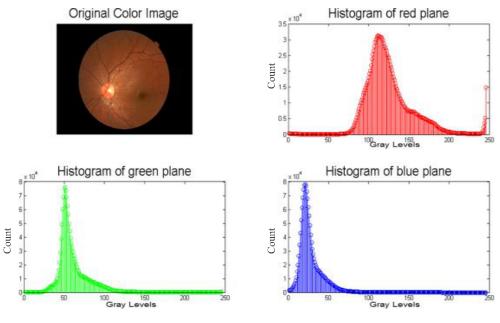
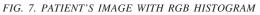


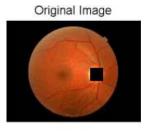
FIG. 6. NORMAL IMAGE WITH RGB HISTOGRAM

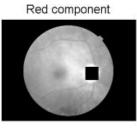




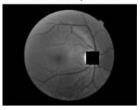
Mehran University Research Journal of Engineering & Technology, Volume 36, No. 4, October, 2017 [p-ISSN: 0254-7821, e-ISSN: 2413-7219] 946

RGB to HSI Conversion: Pre-processed colored image is taken as input and also split into HSI (Hue, Saturation and Intensity) components. Different features are extracted from these components.





Green component



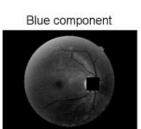
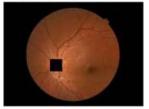


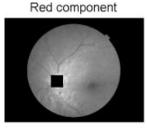
FIG. 8. NORMAL IMAGE WITH RGB COMPONENTS AFTER OD REMOVAL

3.3 **Feature Extraction**

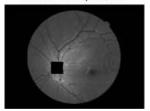
For an automated system to distinguish between normal subjects and subjects with retinal whitening in fundus

Original Image of Patient





Green component



Blue component

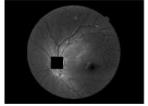


FIG. 9. PATIENT'S IMAGE WITH RGB COMPONENTS AFTER OD REMOVAL

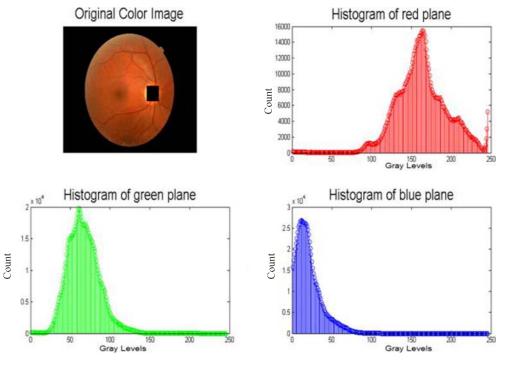


FIG. 10. NORMAL IMAGE WITH RGB HISTOGRAM AFTER OD REMOVAL

images, a feature set comprising various discriminant features has to be formed. The features are extracted from the pixel values. The features have been divided into the following categories.

Grey Level Features: Grey level features are based on the grey scale intensities of RGB components of the RGB image.

Original Color Image

0.5 Histogram of green plane x 10⁴ 100 150 200 50 Gray Levels

Color Based Features: Color based features like HSV.

Statistical Features: Statistical features like mean, standard deviation, entropy and skewness.

Let ü represent an image with m features, then the feature set for each image can be defined by the feature vector v = $\{f_1, f_2, f_3, \dots, f_m\}$. Features are extracted from the fundus

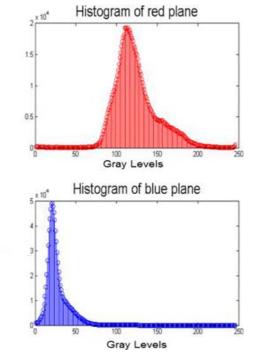


FIG. 11. PATIENT'S IMAGE WITH RGB HISTOGRAM AFTER OD REMOVAL

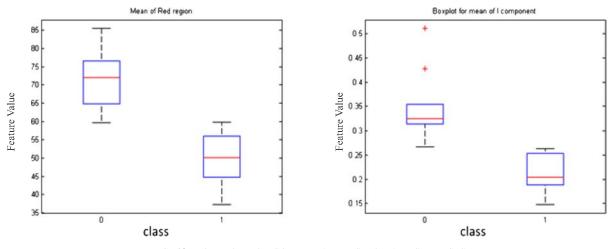


FIG. 12. BOXPLOT FOR SOME FEATURES FOR ALL SUBJECTS

Mehran University Research Journal of Engineering & Technology, Volume 36, No. 4, October, 2017 [p-ISSN: 0254-7821, e-ISSN: 2413-7219]

image after removal of OD pixels and dropping the lowest 10 pixel intensity values. Blue component is not considered for feature extraction as not much discriminant information is available in the blue component.For grading of macular whitening, only the 130x130 region are considered and the same features are computed from this 130x130 area of the image. A total of 48 features are computed from each image. The description of features is explained as under.

- Mean of RGB components of image $f_1 \sim f_3$
- Mean of upper RG regions $f_4 \sim f_5$
- Std. deviation of upper RG regions $f_6 \sim f_7$
- Contrast of upper RG regions $f_9 \sim f_{10}$
- Entropy of upper RG region $f_{11} \sim f_{12}$
- Entropy of lower RG regions $f_{13} \sim f_{14}$
- Skewness of upper RG regions $f_{15} \sim f_{16}$
- Skewness of lower RG regions $f_{17} \sim f_{18}$
- Mean of HSI components $f_{19} \sim f_{21}$
- Std Dev of HSI components $f_{22} \sim f_{24}$
- Contrast of HSI components $f_{25} \sim f_{27}$
- Entropy of HSI components $f_{28} \sim f_{30}$
- Skewness of HSI components $f_{31} \sim f_{33}$
- Top 5RGB intensity values of image. $f_{34} \sim f_{48}$

3.4 Feature Selection

Machine learning systems employ various feature selection methods to select a subset of features that are most relevant for model construction. To avoid the curse of dimensionality at the classification stage and reduce the computational complexity of the classifier, redundant or irrelevant features are dropped and the most relevant features are ranked according to a particular scoring method that reflects the discriminative power of that particular feature. We have used t-test method [4] that calculates p-value of the t-statistic assuming that the means of the two classes are identical. Table 1 gives the results of rank test and p-value score for all the features explained above. Classification parameters are computed for various feature vector length and the most suitable feature vector length is selected for all computations and detailed results are reported for that value.

Fig. 12 shows the boxplot of some features for all subjects. Fig. 13 shows the scatter plot of mean for Index value computed for all subjects.

3.5 Classification

In order to classify an image as a normal image or an image with retinal whitening, supervised learning based classifiers are used. SVM classifier has been used for classification of data. SVMs are supervised learning algorithms which are very useful in separating multidimensional data into two classes. For nonlinear separable data, we have the following equation.

$$d(\mathbf{X}^{\mathrm{T}}) = \sum_{i=1}^{N} \mathbf{y}_{i} \alpha_{i} K(\mathbf{X}_{i}, \mathbf{X}_{j}) + \mathbf{b}$$
(1)

where $K(X_i, X_j)$ is called the kernel function. Here y is class label, α is coefficient and b is biased term. There are different kind of kernels that are used with SVM like Sigmoid kernel, Polynomial kernel of degree h, and Gaussian radial basis function kernel etc. We have used the Radial basis kernel to train our data set due to nonlinearity present in the data and by assuming that distribution is Gaussian. Classification is a two-step process in which the normal subjects and patients are classified in the first step. Once the patients are classified, further grading into macular or other form of whitening is done in the second step.

Feature	Rank Score	p-Value Score	Feature	Rank Score	p-Value Score
7	6.215	0.00001	19	2.024	0.027
9	5.098	0.00021	18	1.807	0.042
24	5.029	0.00025	2	1.805	0.042
27	4.670	0.00059	5	1.805	0.042
1	4.629	0.00065	33	1.795	0.043
4	4.629	0.00065	17	1.618	0.059
11	3.814	0.00047	23	1.615	0.059
3	3.733	0.00047	20	1.592	0.062
6	3.733	0.00047	13	1.164	0.128
42	2.952	0.0036	26	1.156	0.13
43	2.783	0.0054	28	1.003	0.163
44	2.748	0.0058	35	0.995	0.165
45	2.682	0.0068	38	0.934	0.180
46	2.577	0.0085	39	0.869	0.197
8	2.408	0.012	25	0.849	0.202
16	2.398	0.012	41	0.821	0.210
10	2.386	0.013	22	0.665	0.265
29	2.355	0.013	31	0.623	0.269
47	2.310	0.015	34	0.424	0.337
48	2.294	0.015	37	0.310	0.379
30	2.233	0.018	40	0.301	0.383
14	2.211	0.0188	15	0.264	0.397
36	2.199	0.019	21	0.227	0.411
12	2.186	0.019	32	0.107	0.457

TABLE 1. RESULT OF RANK TEST AND P-VALUE SCORE FOR ALL	FEATURES

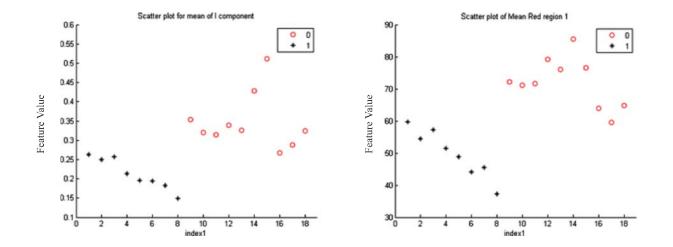


FIG. 13. SCATTER PLOT FOR SOME FEATURES FOR ALL COMPONENTS

Mehran University Research Journal of Engineering & Technology, Volume 36, No. 4, October, 2017 [p-ISSN: 0254-7821, e-ISSN: 2413-7219] 950

3.6 Grading

Detection of Macula: Detection of macular region in the fundus image is important for the classification of whitening region as macular or peripheral. Once the macula in the image is correctly localized, a 130x130 region around the centre of macula is considered. The reason for choosing 130x130 is that the macular a vascular region in used dataset consits of a square region of this size. The process of detection of macula uses the geometry of the OD and the presence of blood vessels. For the proposed algorithm, we have used four features that characterize the macula. These features include area of the macula, distance from optic disc, mean intensity and angle with optic disc. These features are explained as under.

Normalized Area of the Macula (v_1) : This is simply the total number of pixels present in the macula region normalized with some dividing factor.

Distance from Optic Disc (v_2) : Euclidean distance between OD and macula in the form of pixels.

Angle with Optic Disc (v_3) : The angle between OD and macula center along the horizontal axis in radians.

Mean Intensity (\mathbf{v}_4) : Mean intensity of the region for the Green channel.

For the detection of blood vessels, 2D Gabor wavelet is used on the inverted green channel of the fundus image. This is followed by multilayer thresholding for vessel segmentation [22]. OD detection algorithm in [18] has already been explained and the same has been used for detection of the pixels corresponding to OD. Minimum distance classifier and Otsu's algorithm [23] are used to segment the OD and the blood vessels from the fundus image. The features computed for macular region are then used to segment the macula from the fundus image. Using these features and connected component analysis the centre of the macular region is computed. Fig. 14 shows the 130x130 macular region of one of the images and the corresponding RGB components of the region. Fig. 15 shows the 130x130 region and the RGB histogram for each region. Once the 130x130 region is segmented from the macular region, features are calculated for this region using the same methodology as explained in previous section and these features are used for grading of the macular region as having whitening or clear of whitening.

Grading of Retinal Whitening: In the second step, the test samples classified as patients are further classified into subjects with macular whitening or peripheral whitening. SVM classifier is used with Radial basis function for classification. Leave-one-out classification method is used to calculate the classification results.

4. EXPERIMENTAL RESULTS AND DISCUSSION

4.1 Material

To evaluate the performance of the proposed method, a dataset of 22 images has been usedwhich have been

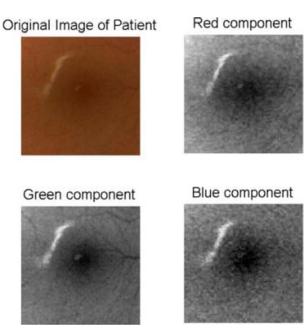


FIG. 14. MACULAR REGION AND ITS RGB COMPONENTS

labeled by a qualified ophthalmologist. Out of the 22 images, 10 images correspond to normal subjects whereas 12 images correspond to subjects with some form of retinal whitening present in the retina. The image dataset contains RGB images with 8 bits per pixel for an image resolution of 1536x2048. The resolution of some of the images in the dataset is different, which are re-sized to 1536x2048 resolution. The class labels of normal subjects and subjects with retinal whitening are labeled by a qualified ophthalmologist. Fig. 16 shows some of the images from the dataset.

4.2 Results

The feature vector extracted from the images dataset contains 48 features. In the first step, we define two classes such as R_1 = Normal subject and R_2 = Patient. The dataset is divided into training data and testing data randomly using 50% data as training data and 50% as testing data. The training data, with class labels, is used for training of SVM classifier using Gaussian Kernel through a supervised classification method. Once the classifier has been trained with the training data, testing data is used to test the performance of the system. The same classification scheme is repeated using 3-folds cross validation and Leave-one-out cross validation methods. Various statistical performance measures are used to calculate the results of classification (Normal or Patient).Results from the classifier have been computed for top 40, 20, 10, 7 and 5 features.

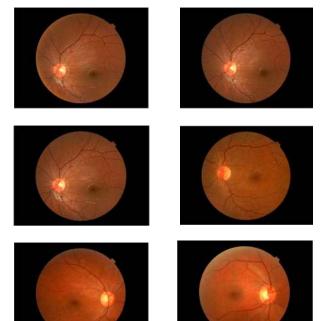


FIG. 16. FUNDUS IMAGES FROM THE DATASET

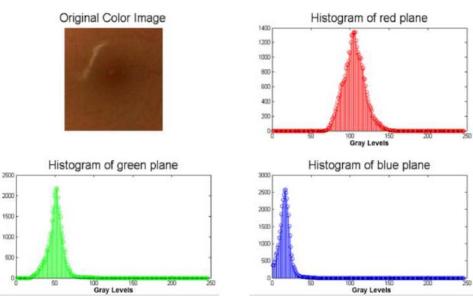


FIG. 15. MACULAR REGION AND RGB HISTOGRAM

For detailed statistical evaluation, the 10 normal subjects in the dataset are labeled as '0' and the 12 patients are labeled as '1'. The images in the dataset are from the AFIO (Armed ForcesInstitute of Ophthalmology) database. The experiments are performed using 3 subsets of data i.e. 50-50, 3-fold cross validation and LOO (Leave-One-Out). The experiments are repeated 100 times for each setup to get unbiased results. SVM classifier is used by selecting the Gaussian Radial Basis Function and calculating the value of sigma through a grid search. For comparison of results with SVM classifier, classification results are been computed using k-NN classifier and Decision Tree classifier.

Classification accuracy, sensitivity and specificity are the performance parameters that have been calculated for the test data set. Sensitivity is true positive rate and specificity is true negative rate. The values of sensitivity and specificity have been calculated using the following equations.

Sensitivity = TP/(TP + FN)(2)

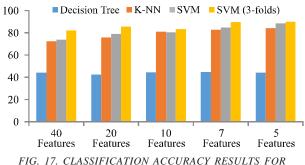
Specificity = TN/(TN + FP) (3)

Accuracy = (TP + FN)/(TP + TN + FP + FN)(4)

WhereTP (True Positives) meaning retinal whitening patients correctly classified, TN (True Negatives) meaning normal subjects correctly classified, FP (False Positives) meaning normal subjects classified as patients with retinal whitening, FN (False Negatives) meaning retinal whitening patients classified as normal subjects, and Accuracy is the number of subjects correctly classified in the given dataset.

The classification accuracy results using different feature vector size and various classifiersare shown in Fig. 17 and Table 2. It shows that proposed system gives best result with top 5 features. 50% training data and 50% test data is used for all classifiers and results are averaged over 100 iterations. The SVM (3-folds CV) results are averaged over 100 iterations. The results for other

classification parameters using top 5 features are reported in Table 2. SVM classifier accuracy using LOO-CV is averaged over 100 iterations. To distinguish between retinal whitening and other abnormalities, abnormal features like hemorrhages, exudates and papilledema should appear normal to this model. In order to test the performance of the model for other abnormalities, 5 images with hemorrhages and exudates are used to test the performance of the classifier and all these images are correctly classified as normal images. Fig. 18 shows 2 of the images used for this purpose. These images show fundus photographs with different abnormalities other than retinal whitening.



VARIOUS FEATURE VECTOR SIZE USING DIFFERENT CLASSIFIERS (50% TRG DATA & 50% TEST DATA)

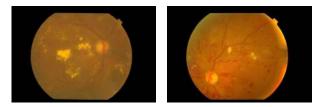


FIG. 18. FUNDUS IMAGES WITH ABNORMALITIES (OTHER THAN WHITENING)

TABLE 2. CLASSIFICATION PARAMETERS FOR VARIOUS							
CLASSIFIERS USING TOP 5 FEATURES (ALL RESULTS							
IN PERCENTAGES)							

Parameter	Decision Tree	k-NN	SVM	SVM (3-folds)	SVM (LOO)
Specificity	70	91.3	85.59	92.0	-
Sensitivity	39	80.68	93.43	90.27	-
Acc	44	88.44	88.44	89.89	95.0

5. **DISCUSSION**

The evaluation of proposed system is carried out using different number of features and classifiers i.e. decision tree, k-NN and SVM with different cross validation settings. It gives best accuracy of 95% for top 5 features and SVM using LOO settings. SVM outperformed other classifiers due to the inclusion of RBF kernel along with SVM with transforms nonlinear data into a linearly separable space. Secondly LOO proved to be best setup in this scenario due to less number of effected images as compared to normal ones. We further used the proposed model for sub grading of retinal whitening as macular and peripheral whitening. This grading is carried out using macula detection as explained in proposed method. We took 12 subjects out of which 3 subjects with macular whitening are labeled as '1' and 9 patients with peripheral whitening are labeled as '0'. Trained SVM model with RBF kernel is used and experiments are performed using the top 5 features with LOO-CV methodology. 100% classification accuracy is achieved over 100 iterations for this grading which means proposed model always graded these 12 subjects correctly.

6. CONCLUSION

Cerebral malaria is a disease that can be detected and properly treated if an early diagnosis is done. The proposed Decision Support System can provide such a benefit where an ophthalmologist is not available. In this study we propose a system for early detection and grading of cerebral malaria based on retinal whitening in fundus image. This bio-marker of retinal whitening was not used before and the results achieved from the proposed model are very encouraging. The color and statistical features from the red, green and HSI component of the fundus image provide enough discriminatory data to achieve a classification accuracy of upto 95% on the given dataset. The computer model generated has good robustness and performs well for other abnormalities like exudates and hemorrhages and these abnormalities do not affect the performance. For the grading part, all subjects with macular whitening were correctly identified from the dataset containing cases of peripheral whitening as well.

In summary, we propose a complete computed aided diagnostic and decision support system that is trained on the feature set extracted from the fundus images and very few features provide a robust and accurate assessment of the presence of retinal whitening and the system could be integrated into a clinical diagnosis system to assist ophthalmologists for early diagnosis of cerebral malaria.

ACKNOWLEDGEMENT

This research was funded by National ICT R&D fund and medical data and annotations are gathered with the help of ophthalmologists from Armed Forces Institute of Ophthalmology.

REFERENCES

- Sithole, H.L., "A Review of Malarial Retinopathy in Severe Malaria", African Vision and Eye Health, Volume 70, No. 3, pp. 129-135, 2011.
- [2] Abràmoff, M.D., "Automated Early Detection of Diabetic Retinopathy", Ophthalmology Volume 117, No. 6, pp.1147-1154, 2010.
- Faust, O., "Algorithms for the Automated Detection of Diabetic Retinopathy using Digital Fundus Images: AReview", Journal of Medical Systems, Volume 36, No. 1, pp. 145-157, 2012.

- [4] Akram, M.U., Khalid, S., Tariq, A., and Javed, M.Y.,
 "Detection of Neovascularization in Retinal Images using Multivariate M-Mediods Based Classifier", Computerized Medical Imaging and Graphics, Volume 37, No. 5, pp. 346-357, 2013.
- Zitnick, C.L., and Sing, B.K., "Stereo for Image-Based Rendering using Image Over-Segmentation", International Journal of Computer Vision, Volume 75, No. 1, pp. 49-65, 2007.
- [6] Chawla, N.V., Nathalie, J., and Aleksander, K., "Editorial: Special Issue on Learning from Imbalanced Data Sets", ACM Sigkdd Explorations Newsletter, Volume 6, No. 1, pp. 1-6, 2004.
- [7] Joshi, V.S., "Automated Detection of Malarial Retinopathy-Associated Retinal HemorrhagesAutomated Detection of Malarial Retinopathy", Investigative Ophthalmology &Visual Science, Volume 53, No. 10, pp. 6582-6588, 2012.
- [8] Tang, L., Niemeijer, M., Reinhardt, J.M., Garvin, M.K., and Abràmoff, M.D., "Splat Feature Classification with Application to Retinal Hemorrhage Detection in Fundus Images", IEEE Transactions on Medical Imaging, Volume 32, No. 2, pp. 364-375, 2013.
- [9] Sinthanayothin, C., Boyce, J.F., Williamson, T.H., Cook, H.L., Mensah, E., Lal, S., and Usher, D., "Automated Detection of Diabetic Retinopathy on Digital Fundus Images", Diabetic Medicine, Volume 19, No. 2, pp. 105-112, 2002.
- [10] Hatanaka, Y., "Improvement of Automatic Hemorrhage Detection Methods Using Brightness Correction on Fundus Images", Medical ImagingInternational Society for Optics and Photonics, pp. 69153E-69153E, 2008.
- [11] Lee, S.C., Lee, E.T., Wang, Y., Klein, R., Kingsley, R.M., and Warn, A., "Computer Classification of Nonproliferative Diabetic Retinopathy", Archives of Ophthalmology, Volume 123, No. 6, pp. 759-764, 2005.

- [12] Hoover, A., and Michael, G., "Locating the Optic Nerve in a Retinal Image using the Fuzzy Convergence of the Blood Vessels", IEEE Transactions on Medical Imaging, Volume 22, No. 8, pp.951-958, 2004.
- [13] Walter, T., Klein, J.C., Massin, P., and Erginay, A., "A Contribution of Image Processing to the Diagnosis of Diabetic Retinopathy-Detection of Exudates in Color Fundus Images of the Human Retina", IEEE Transactions on Medical Imaging, Volume 21, No. 10, pp. 1236-1243, 2002.
- [14] Niemeijer, M., Michael, D.A., and van Ginneken, B.,
 "Information Fusion for Diabetic Retinopathy CAD in Digital Color Fundus Photographs", IEEE Transactions on Medical Imaging, Volume 28, No. 5, pp. 775-785, 2009.
- [15] Sopharak, A., Uyyanonvara, B., Barman, S., Vongkittirux, S., and Wongkamchang, N., "Fine Exudate Detection Using Morphological Reconstruction Enhancement", International Journal of Applied Biomedical Engineering, Volume 1, No. 1, pp. 45-50, 2010.
- [16] Osareh, A., Shadgar, B., and Markham, R., "A Computational-Intelligence-Based Approach for Detection of Exudates in Diabetic Retinopathy Images", IEEE Transactions on Information Technology in Biomedicine, Volume 13, No. 4, pp. 535-545, 2009
- [17] Yazid, H., Arof, H., and Isa, H.M., "Automated Identification of Exudates and Optic Disc Based on Inverse Surface Thresholding", Journal of Medical Systems, Volume 36, No. 3, pp. 1997-2004, 2012.
- [18] Yasmin, K., Tariq, A., and Akram, M.U., "A Comparison and Evaluation of Computerized Methods for OD Localization and Detection in Retinal Images", International Journal of Future Computer and Communication, Volume 2, No. 6, pp. 613-618, 2013
- Wang, H., Hsu, W.G., and Lee, M., "An Effective Approach to Detect Lesions in Colour Retinal Images", Proceedings of IEEE Conference on Computer Vision and Pattern Recognition, Volume 2, pp. 181-187, 2000.

- [20] Quellec, G., Lamard, M., Josselin, P.M., Cazuguel, G., Cochener, B., and Roux, C., "Optimal Wavelet Transform for the Detection of Microaneurysms in Retina Photographs", IEEE Transactions on Medical Imaging, Volume 27, No. 9, pp. 1230-1241, 2008.
- [21] Salam, A.A., Tehmina, K., Akram, M.U., Jameel, A., and Basit, I., "Automated Detection of Glaucoma Using Structural and Non-Structural Features", Springer Plus, Volume 5, No. 1, pp. 1519, 2016.
- [22] Akram, M.U.,Khalid, S., Tariq, A., and Javed, M.Y., "Detection of Neovascularization in Retinal Images using Multivariate M-Mediods Based Classifier", Computerized Medical Imaging and Graphics, Volume 37, No. 5, pp. 346-357, 2013.
- [23] Gonzalez, R.C., and Richard, E., "Digital Image Processing", Prentice Hall Press, [ISBN:0-201-18075-8], 2002.