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Detection of Pemphigus Vulgaris in Development Stage of Skin Erosion

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Abstract. Pemphigus Vulgaris (PV) is an autoimmune blister disease which is a common type of pemphigus. It is involved in the oral mucosa and skin area. Some facts are making the diagnosis of PV disease even more difficult. Only one characteristic is identifying the PV blister that is Nikolsky's sign (bulla spread sign). PV blister looks like the same as the other blister disease. Rupture blister makes erosions on the surface of the skin area. The clinical diagnosis of PV is more painful. Therefore, selecting an area of relevant diagnosis procedure is most important not just for dermatologists but for non-expert person as well. The proposed work is an attempt to provide a solution for the detection of PV in the development stages of skin erosion. We explore a systematic and effective framework system for identifying PV from relevant information, image data, and the description. Our system works on two-section, first is interrogation about symptoms and second different types of image analysis to detect blister images. The system successfully detects PV blister with an accuracy rate of 88.67%.

Keywords: Pemphigus Vulgaris, Auto immune disease, Blister, Skin disease, Expert System, classifier, Random forest.

1 Introduction

Blister (Bulla) skin diseases are a group of autoimmune disorders. Pemphigus Vulgaris (PV) is one of the blister diseases. The life-threatening of PV diseases affect 1 to 5 patients per 1,000,000 populations per year [1]. PV can prove to be a serious fatal disease if it is untreated. The majority occurrence found in between 40 to 60 years of age [2]. The occurrence ratio in women is higher compared to men and the ratio range from 1:2 [3]. In 70–90% of the cases it presents itself with painful and long-persisting erosions and blisters of the mucous membranes, especially of the oral mucosa that afterward will spread in another body area [4]. On the skin, PV is characterized by widespread fluid-filled blisters that arise on normal-appearing skin and are finally ruptured to evolve into superficial erosions. It has an important symptom which is bulla spread sign. In the active phase of PV, It is characterized by the epidermal detachment caused by the pressure at the edge of a blister, it is also known as Asboe –

Hansen sign or Nikolsky's sign [5]. The PV distribution is geographically unequal. Worldwide - The ranges from 0.76 in Finland, 3.5 in Japan, and 16.1 in Jerusalem the new cases per million in the year [5].

The proposed system provides an approach for the detection of PV. We have developed the questionnaire in the form of an expert system. The expert system is user friendly and can be used by technical and non-technical users leading to a rise in efficiency, effectiveness, and successive productivity in the diagnosis of PV.

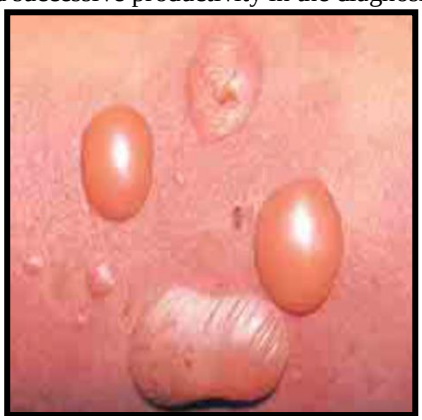


Fig. 1. Skin area blister

1.1 Literature survey

We studied different research papers of technical and biomedical for the detection of PV disease. Several researchers have purposed the image analysis techniques to detect various types of skin diseases. We briefly review some of the techniques reported in the literature survey.

Schlesinger et al., in their work of "Nail involvement in pemphigus Vulgaris [6]" study on 64 patients with PV disease. They found that nail changes in 30 out of 64 PV patients; with 14 patients having biopsy-proven PV of the nail. Habibi et al., in their work of "Nail changes in pemphigus vulgaris [7]", found that 25 out of 79 PV patients had nail changes during the occurrence of PV disease.

In 2006, Iamaroon, et al., in their work "Characterization of oral Pemphigus Vulgaris in Thai patients [2]", illustrated a robust and automated method for the diagnosis of skin diseases. They examined 18 patients with the oral blister. Here identify the characteristics of patients and lesions in 18 cases of oral PV. The mean age was 38 years for these 18 cases, and the male: female ratio was 1:2.

In 2017, Sohel Tavakolpour, et al., in their work "Pemphigus trigger factors: special focus on Pemphigus Vulgaris and pemphigus foliaceus [8]", illustrated that a pemphigus inducers are a significant number of reported cases, certain forms of drugs and treatments. They examined that many causes have been addressed, including numerous drugs and treatments, illnesses, vaccinations, genetic factors, nutrients, micronutrients, childbirth, stress, and other triggers.

In 2008, T Shamim, Vengal, et.al, in their work of "Pemphigus vulgaris in oral cavity: Clinical analysis of 71 cases [1]". They study and evaluate in their case report the patients of PV in the oral area. They survey on the 71 cases of PV over 7 years. Get the clinical details of the patient such as age, sex, oral lesions, oral duration, and oral involvement during the blister. They get the result of about 53.52% of 71 cases. And they found the oral was the initial area of involvement during the PV disease. The average age was 42.73 years.

In 2014, V Sharon Baum, et al., in their work, "Diagnosis and classification of autoimmune blister diseases [4]", stated that they classify the autoimmune blister diseases based on blister formation by the epidermis, the dermal junction of blisters, and erosions on the skin. After the examined the blister they classify pemphigus and pemphigoid groups of blister diseases.

In 2016, S. Kolkur and D.R. Kalbande, survey on the "Survey of Texture Based Feature Extraction for Skin Disease Detection [9]". Texture based feature extraction for the detection of skin diseases. It is computed from the statistical distribution of particular positions in the image. The intensity points as pixels in each combination and statistics are classified into different orders as the first-order, second-order, and higher-order statistics. They use the GLCM method; it is a way of extracting second-order statistical texture features. The Last and higher-order, textures consider the relationships among three or more pixels. At Last, Classify the image as skin disease or not with neural networks and SVM classifiers.

In 2017, U. Ansari and T. Sarode, in their work "Skin Cancer Detection Using Image Processing [10]", proposed the detection of skin cancer identification with SVM. Use Image processing techniques for diagnosing then applied the segmentation of thresholding, GLCM techniques, and extract the feature. At the last, use the SVM classifier for the classification of the image as non-cancerous or cancerous.

In 2016, S. S. K, et al., in their work "Dermatological Disease Detection Using Image Processing and Machine Learning [11]", proposed a two-stage approach that is Computer Vision and Machine Learning. In the first stage of computer vision, apply pre-preparing procedures, and feature extraction. Machine learning is the second stage, for examining the skin. They test on the six diseases with 95% accuracy.

In 2014, J. K, J. B "Detection of Malignant Skin Diseases Based on the Lesion Segmentation [12]", represents the technique to detect the skin diseases using a conventional camera. The aim of the algorithm is an early diagnosis of malignant diseases. The proposed works for pre-processing step with images by taking the HSV color component. For detection, the lesion segmentation step is performed. Use morphological features as the asymmetry, detect the border irregularity, different color variation, and use diameter. These extracted features and identify malignant lesions or non-malignant.

In 2016, Fazly Salleh Abas, et al., in their work, "Acne image analysis: Lesion localization and classification [13]", stated the analysis of acne images. The first producer on filtering, thresholding, and then apply feature extraction with the acne lesion image. Used different classifiers like a binary classification tree, discriminate analysis classifier, K-Nearest Neighbor classifier, and Naïve Bayesian classifier.

In 2015, A.A.L.C. Amarathunga, et al., in their work “Expert System for Diagnosis of Skin Diseases [14]”, this framework utilizes such as image processing and data mining for the finding of the malady of the skin. They have done different pre-processing tasks and effective noise removal noise of the images. The images are segmented by threshold values that will divide the image in two sub-parts. At the last, data mining systems are utilized to distinguish the skin ailment.

In 2018, V. Zomnrylü, et al., in their work “The Quantitative Assessment of Progressive Dermatologic Manifestations in Selected ROI (Region of Interest) [15]”, stated that developed the algorithm for detecting the blister lesions. It represents a unique attempt to develop a systemized mathematically based technique of detecting targeted blister lesions affected skin areas.

From the literature survey, we have identified some issues:

The color after the burst of PV blister is identical to the burnt color: The burst blister rupture that burns is severe, the burn blister may be dry, leathery and the color is red, black, brown, or white. That blister and the rupture blister area are visually the same as the PV blister and the erosions.

PV blisters are identical to other autoimmune skin blisters [7]: The human body’s immune system by mistakes for something it attacks this healthy skin tissue. This causes many autoimmune diseases to appear on the different body are and blister disease one of them. Blister appears on the skin upper area. All autoimmune blisters are visually the same as another blister and covered by the fluid-filled bubble.

PV initiates within the oral area and spread in other parts of the body within the sort of skin erosions [8]: Blisters in the mouth quickly ruptured to form erosions. There may be one or several or join together. Oral area lesions may be the one sign for an average of 5 months before skin lesions develop. After that, blister spread in the different body area that's why we need a different specialist in different stages.

The identification of significant symptoms of PV i.e. Nikolsky’s sign [5]: The autoimmune blisters are visually the same as another blister, but that blisters have a unique key factor to identify. So in PV have also a unique key factor "Nikolsky’s sign". The PV patients have characteristic of nikolsky’s sign with active blistering, the pressure with a finger applies on the blister separates from the normal epidermis, and after the ruptured blister, and it was producing erosions. This sign is not specific for PV blistering diseases.

Some Blister patients do not visit the doctor at the appropriate time and some blister patients have difficulties to communicate with the doctor about their health issues. From identified some issues we proposed to attempt and provide a solution for the detection of Pemphigus Vulgaris in developmental stages of skin erosions.

1.2 Description of Database.

We collected our image database from different websites specific blister diseases and collected from the medical expert. The database has 330 images (47 PV blister images, 76 Non-PV, 117 PV Augmentation images, 109 Non-PV Augmentation images).

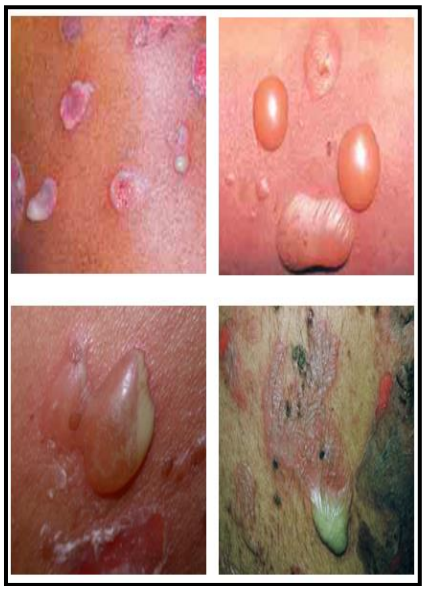


Fig.2. PV blister image

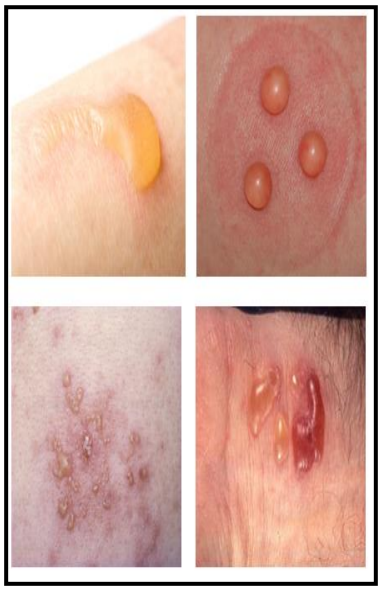


Fig.3. Non-PV blister image

1.3 Technical Assessment for PV identification

From the literature survey, we identified that we need a computerized system to detect PV or Not-PV disease. We design an expert system and image processing; both are very useful to deals with each other to detect the PV disease. We have visited clinics and collect responses and blister images from patients and design some questions. For image analysis, we tested on 150 real images in this research. Fig.4 is the flowchart of the proposed system.

We differentiate two sections Primary and Secondary. In the Primary section, we present the expert system, developed questions for interrogation of symptoms using a computer system. The patient will answer those questions according to his experience of PV blister. Every question gave some weight-age. Criteria will be determined based on the answers to the questions given by the patient. If the criteria are satisfied then the phase of image analysis will come. But if the criteria are not satisfied, then we will be suggested for a skin biopsy to patients.

The secondary section is the image analysis; we extract meaningful information from the digital image. The image analysis has sub-tasks that are such as Pre-processing, segmentation, Extract ROI and feature extraction, classification. By the Texture feature, we can classify the PV blister image. In the end, after performing all the operations, we classified the blister as “PV” or “Not-PV”. Thus, this way effective for the detection of PV to the computerized domain.

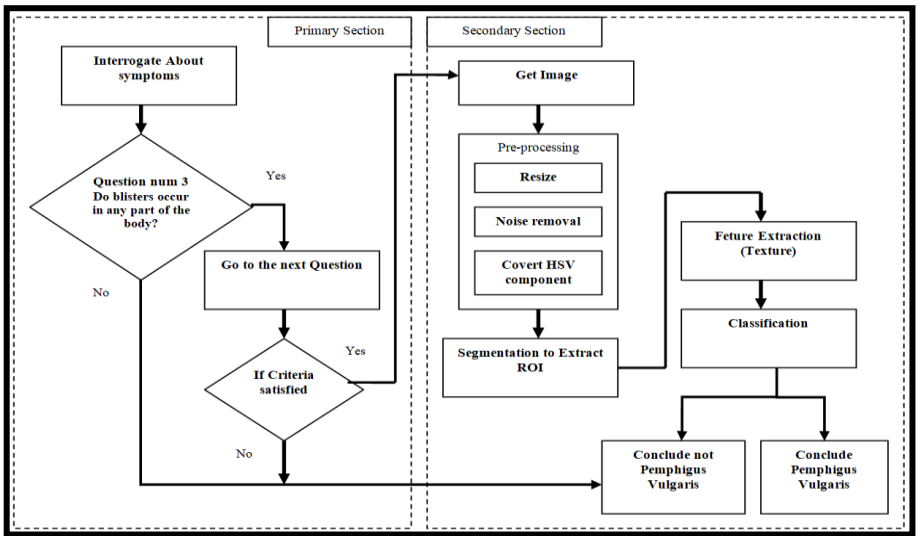


Fig.4. Step to detect PV Blister on skin

Primary Section/ Interrogate About symptoms

The Primary step is "Interrogate About symptoms" with the expert system. The questions are such as a questionnaire regarding the characteristics of PV blister to patients.

The purpose of doing this questionnaire is there are so many types of blister for various skin diseases that are similar to the appearance. For this reason, the diagnosis task very difficult. We collected the patient's response, designed some questions, and consulting the medical expert. All blisters have unique characteristics that make PV distinguishable from other blister diseases. Few general characteristics make PV distinguishable from other blister diseases. All questions are based on PV symptoms. The questions depend on the previous question of the answer. The system performs diagnosis for PV patients by asking questions related to the conditions that require objective answers. The system suggests the user chose the answer.

In which the symptoms of There is a high chance of PV disease are more prevalent, and then those options have been given more weight-age. Some alternatives may or may not have symptoms of PV disease then those options have been given average weight-age. In those where the symptoms of PV disease are less prevalent, those options are given a lower weight-age.

The system calculates and gives the symptoms match to the patient. If the basic requirement of the characteristics of PV blister disease is not satisfied, then there is no point for going further into the image processing section.

Here the ratios are given. This ratio is taken bases on 100 patients. The weight-age is given based on how many people are affected.

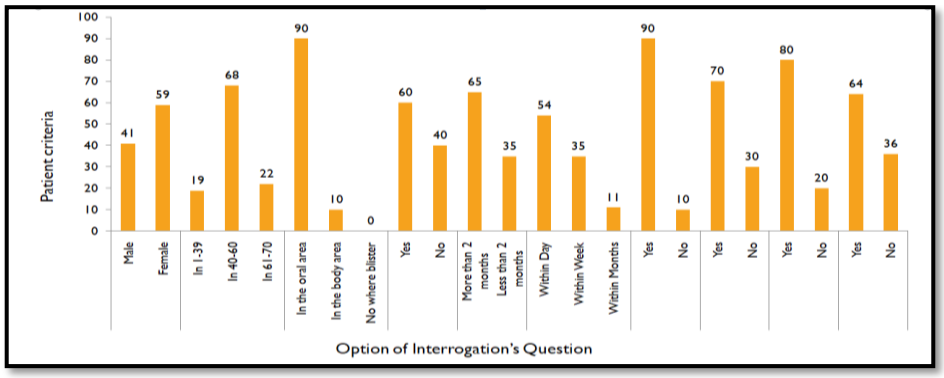


Fig.5. Representation of Patient ratio

If all the criteria are satisfying then, the system will calculate the patient's answer and give the percentage. After the result, the image analysis part comes. Here the primary step will complete.

Table 1. Questionnaire of interrogation about symptoms

NO	Question	Options	Weight
1	The gender of the patient	Male	8
		Female	10
2	What is the age of the patient?	In 1-39	8
		In 40-60	10
		In 61-70	2
3	Where blisters first appeared?	In the oral area	10
		In the body area	2
		No, where blister	0
4	Whether blisters are present in the Stomatitis area	Yes	10
		No	8
5	A period of blisters in the oral area	More than 2 months	10
		Less than 2 months	2
6	How much time taken for rupturing of blisters	Within Day	10
		Within Week	8
		Within Months	2
7	Whether flaccid arose on healthy skin while rupturing blisters?	Yes	10
		No	2
8	Having itching problem or not?	Yes	2
		No	10
9	Nails are affected?	Yes	10
		No	8
10	Is there any maceration in skin folds?	Yes	10
		No	8

Secondary Section / Image Analysis

After the criteria get satisfied, the next step is the image analysis of the blister image given by the patient. The patient can give the image of the blister in two ways. First, capture images using a camera and second, from the database.

Image analysis extracts meaningful information from digital image form processing techniques. Many different techniques are used in image analysis. Each technique is useful for a range of tasks in different fields of image analysis. Our images are taken under different clinical conditions, different skin tone, and at different stages of illness development with and various colors, sizes, the shape of the blister. We developed a clinically applicable, effective system for automated detection of PV blister. We have visited clinics, communicate with the organization, Expert and from the online sources, we collect blister images from them and tested on 89 real images. The results are present in Fig.6.

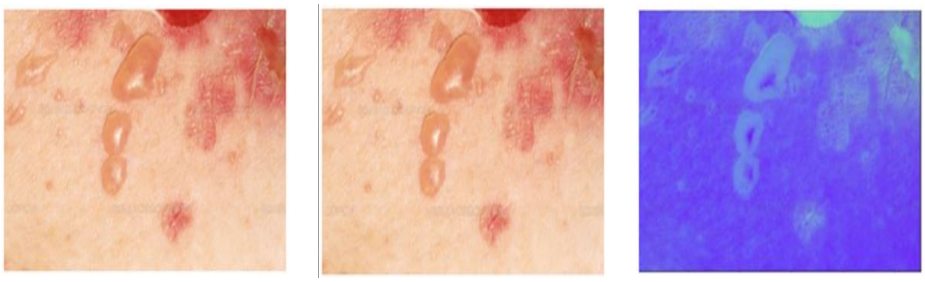
Pre-processing is the primary step. After the get image form user, the next task is pre-processing. Every image is not in the precise size. We standardized sized to a species that's 400/400. While image processing, noises are produced. For the smooth image, remove unwanted noise. So after doing resizing, the next task is to enhance the image so that the improved the quality of the image.

We use a Gaussian blur filtering. The Gaussian noise each noisy a pixel within the image is the summation of the correct pixel value, and arbitrary Gaussian distributed value. This we make our system work more efficiently, with resizing and noise removal operation is carried out. The Color space we have considered is HSV. Convert RGB components into the HSV components which are hue, saturation, and intensity components. Then differentiate the image between hue, saturation, and intensity components. Out of HSV components, the saturation component gives the best result.

After the noise removal process of the image, the next step is image Threshold. It is the simplest method of segmentation. It is simple and effective to separate the background and foreground or isolates objects in the image. With the help of a threshold, the blister will appear with the foreground part.

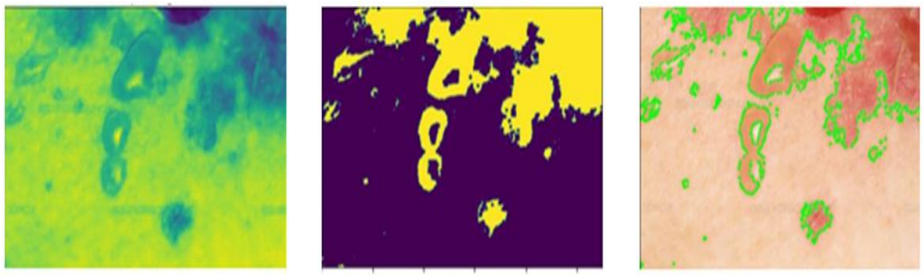
After the segmentation, we apply the contour. It will join the line to all the points along the boundary of the image that are having the same intensity. It comes handy in finding the size of the object of interest and object detection. In this work, the contour draws the boundary line of the blister shape. We set the region of interest (ROI).

An ROI, samples identified for a selected purpose. That blister will detect with the ROI. Fig.7 shows the final results generated by the application of the proposed background and blister extraction method on the original images shown in Fig.7 with the extracted blister highlighted in green. After get ROI, the next step is extracting the useful feature which can classify the input image as PV or Not-PV. Important features are color, shape, and texture for the detection of PV blister.



a b c

Fig.6. (a) Selected original images from the gallery or capture: “Get image”. (b) Use Resize and Noise removal Operation on images. (c) Convert into components of HSV components that are hue, saturation, and intensity



a b c

Fig.7. (a) Difference image between hue, saturation, and intensity components. (b) Segmentation images. (c) The original image with the extracted blisters and highlighted in green color.

We collected the PV blister features to detect PV; we have to map those features and convert them into technical features. We have extracted texture-based from the segmented image for classifying the input image as PV or Not-PV. We are focus on texture features. For classification the objects based on texture, the consistent spread of patterns, object - the object’s surface, Rough-Smooth, Hard-Soft, Fine-Coarse, and the other many such texture pairs, with the help of texture features, easy to classify the image. The next step is to classification it as PV or Not-PV. We apply the number of classifiers such as Random Forest (RF), Support vector machine (SVM), K-nearest neighbor, binary tree. Out of them for classification, the random forest was finalized.

1.4 Result Analysis

In each phase of our system, we worked on two different sections: The first section is Interrogation about symptoms as the Primary section that is questioner’s scenarios and the second section is image analysis. In the primary section, collected the patient’s response and the questions are formulated. There are only objective answers

to all the questions. In all objective answers, some criteria have been set. The patient will answer the questions from experiences about the blister period.

At the last of primary section, if the criteria of the patient's selected options are calculated to be 50% or less than 50%, then the patient does not have symptoms of PV, so we will suggest a biopsy. And if the criteria of the patient's selected options are calculated to be more then 50%, then the patient has symptoms of PV, so we will suggest for upload the image of blister for the image analysis. After the Primary section next is the Secondary section as an image analysis. In our work were done these steps: get image, pre-prospering, segmentation, feture extraction blister analysis, and the classification of PV blister.

At the last of secondary section, we classified the images as PV blister images or Non-PV blister images. The results of 5 fold cross-validation applied on 150 images. 30 images in 1 fold are shown in Table 2 fold cross-validation is shown.

Table 2. Results of 5 folds cross validation

Total 150 Images and 30 Images in 1 Fold						
	Correctly Classified			**Misclassified**		
Cross fold	**SVM**	**RF**	**CART**	**SVM**	**RF**	**CART**
1	20	24	23	10	6	7
2	19	26	21	11	4	9
3	17	22	23	13	8	7
4	21	25	22	9	5	8
5	25	26	26	5	4	4

Fold accuracy of all the classifiers is described in Table 3, where RF has a maximum accuracy of 87% is proved to be better among our system.

Table 3. Fold Classification Accuracy (%)

Cross fold	**SVM**	**RF**	**Cart**
1	66.66%	80%	76.66%
2	63.33%	86.66%	70%
3	56.66%	73.33%	76.66%
4	70%	83.33%	73.33%
5	83.33%	86.66%	86.66%

In the classification algorithm, a confusion matrix is summarizing the performance. Calculating a confusion matrix gives a better result of classification model is getting right or it is making types of errors.

Table 2. Confusion matrix RF, SVM, CART

	ACTUAL					
	RF		SVM		CART	
PREDICTION	64	10	45	29	62	12
	7	69	14	62	11	65

Graphical representation of the Confusion matrix based on the True positive, True negative, False positive, and false negative in Fig. 8.

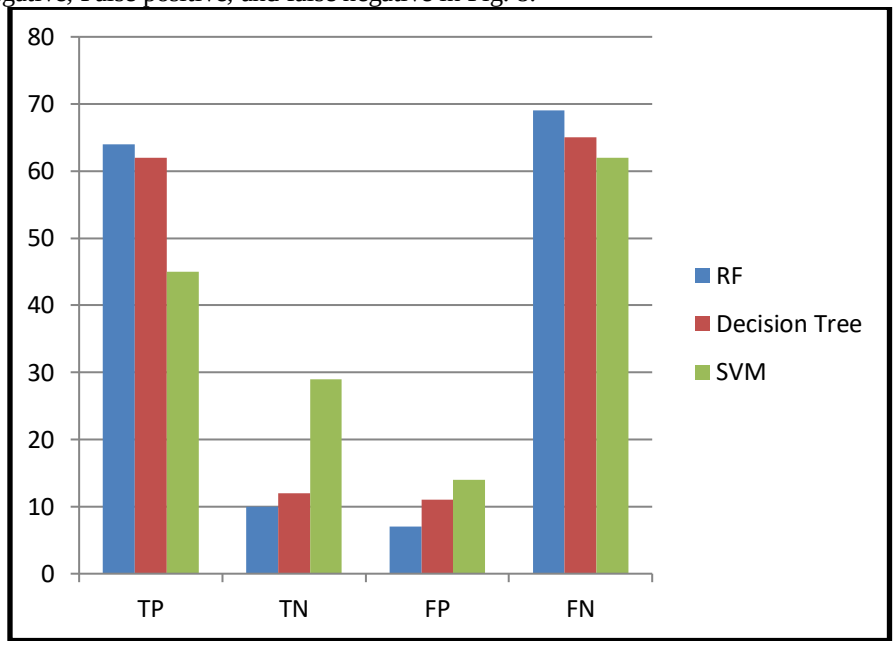


Fig. 8. Representation of Confusion Matrix

We classify the image as PV or Not-PV with the Random Forest (RF), SVM, and binary tree and at the last compare the image with the extracting textures. Out of them, the RF was finalized. Because the RF classifier will handle the missing values. Maintain the accuracy of a large amount of data. It won't allow over fitting in the model. RF handles a large data set with the higher dimensionality. RF has produced a good result for our system. So Graphical representation of the overall accuracy of the classification is described in Fig.9 where RF has a maximum overall accuracy of 88.67% and proved to be better among all for our work.

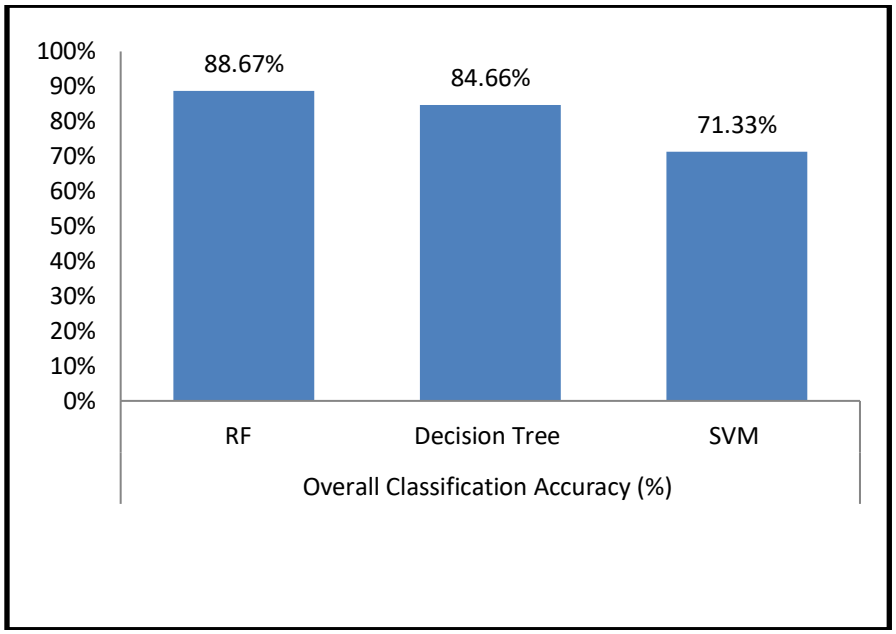


Fig.9. Overall classifier's Performance

So our system has been tested with different scenarios First is if the system does not get any true skin color in the image, then the system gives the notification for the wrong image. The notification is "No, where to get the true skin color, please check your image", "Try again".

Second is if blisters absent and criteria satisfied but with the user upload the wrong image. Example, the image is human skin. But in the image has no blister. For the PV detection blister is compulsory. If the user uploads the wrong image then the system will start the further process but the system will identify the image at the ROI step. The blisters are not available in the image.

Table 5. Recall and Precision of incorrect input

Scenario	No of Image	Recall	Precision	Accuracy
Not Submit the human skin image	20	0.88	0.88	0.90
Submit wrong image after satisfying the criteria	25	0.90	0.83	0.88

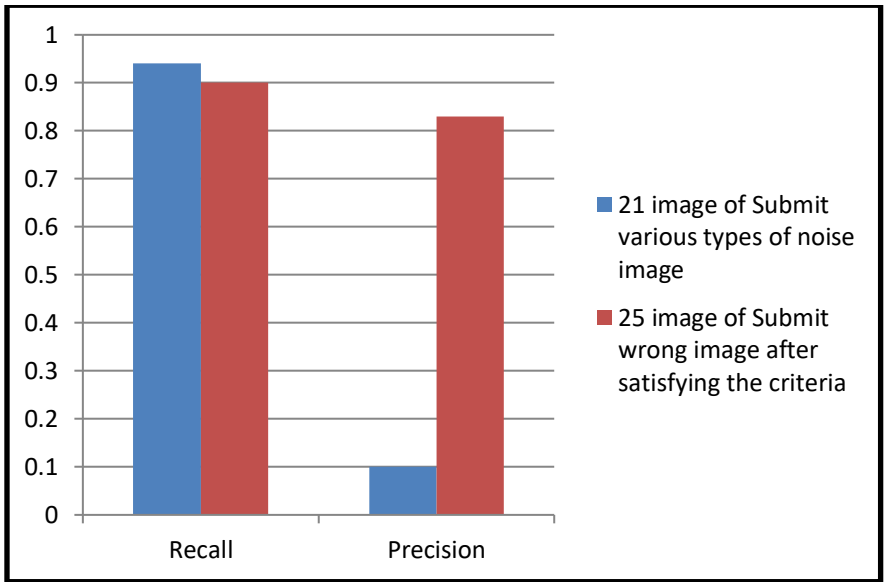


Fig. 10. Graphical Representation of Recall and Precision of incorrect input image**.**

In the Third Scenario, The images have various types of noise. Noise is kind of the result of errors. By noise in image pixel values that do not reflect with the true intensities of the real pixels. There are different ways that noise can be introduced into an image. Example, the image acquisition step and translation step. In the fourth Scenario, the patient gives a variation in image resolution. Each pixel of the image has a different color from its neighbours. As a viewer the image pixels have a distance, these pixels seem to blend together to form the image. Get glitch images and loss the important pixels.

Table 6. Recall and precision of submit various quality of image

Scenario	No of Image	Recall	Precision	Accuracy
Submit various types of noise image	21	0.94	0.1	0.95
Submit wrong image after satisfying the criteria	25	0.90	0.83	0.88

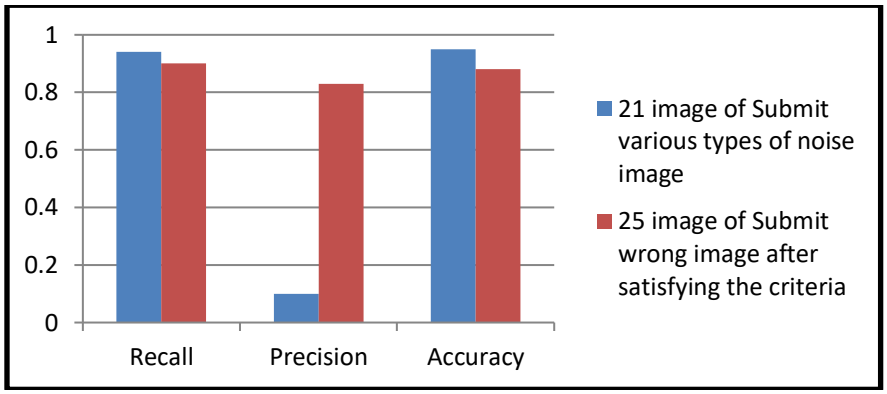


Fig. 11. Representation of Recall and Precision of submit various quality of image

1.5 Conclusion

PV is one of the rare autoimmune blister diseases. We study different literature survey of such as biomedical research papers on PV diseases, we identified that due to painful PV blisters, develop on the skin of the mouth, nose, throat, and genitals. If PV cannot be cured then it will lifelong serious condition or life-threatening. Also, due to its similar kind of characteristics with other blister diseases, it often gets misdiagnosed. Thus, the need for detection of PV in a computerized way.

The PV relevant diagnosis was important not just for dermatologists only but also for dentists. The detection of PV blister even more difficult because it blisters is an autoimmune disease so in various diseases blisters are occurs in the body area. For PV detection needs the main and the basic symptoms of PV. For this, we add two basic task expert system identification and image analysis. The expert system is an identification task. In the image analysis task, Clinical detection of blister represents a challenge with the rupture area, lesions, and other erosions on the surface.

In this paper, we have two section primary as interrogate about system and secondary section classify the detection of PV base on analysis of the image. After the image analysis, in classification, phases one is training and the second is the testing phase. The total number of 123 authentic images collects with various sources. Then we done augmentation on the image and make it 330. Out of 330 images, 180 images are considering the training phase and remain images considered for the testing phase. The results analysis was carried out in different technique scenario and the system provided 88.67% accurate results

For this reason, we develop the system for the autoimmune blister diseases to easy to diagnose and applied to blister affected patient's images taken under various environmental conditions. This system shows various appearances with unique skin tone and color, various sizes and shapes, and the intensity level of the blister. We differentiate and detect the blister skin area, and helpful for non - technical and technical person to detect the PV blister. The future, the future, the system can be extended for the detection of the other blister disease.

1.6 Reference

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