Biochem. Cell. Arch. Vol. 21, No. 1, pp. 1211-1216, 2021	www.connectjournals.com/bca	*ISSN 0972-5075*
DocID: https://connectjournals.com/03896.2021.21.1211		*eISSN 0976-1772*

DIAGNOSIS, TREATMENT AND CLASSIFICATION OF COVID-19 DISEASE BY COMPLETE BLOOD TEST

Qutaiba Mohammed Al Dulaimee[1], Hanan M. Ali*[2], Saad Shaheen Hammadi[3] and Zainab A. Khalaf[4]

[1]Rania Hospital, Al Sulaimania, MOH, Iraq,
[2]Department of Chemistry, College of Education for Pure Sciences, University of Basrah, Iraq.
[3]University of Basrah, Iraq.
[4]Department of Mathematics, College of Science, University of Basrah, Iraq.
*e-mail : hanan1910@hotmail.co.uk

(Received 8 November 2020, Revised 14 January 2020, Accepted 25 January 2021)

ABSTRACT : Currently, there are no approved specific antiviral agents for novel coronavirus disease 2019 (COVID-19). Currently, in spite of the outbreak worldwide coronavirus disease 2019 (COVID-19), still there are no approved specific antiviral. In this study, the 44 patients symptomatically diagnosed COVID-19 were selected randomly from Rania Hospital, Al Sulaimania, north of Iraq. These patients were tested using a complete blood count (CBC) test before and after treatment using different types of drugs with a period of roughly 21 days. Several parameters were measured using the CBC test in order to measure the varying degrees of variables before and after treatment. The results showed a significant decrease in lymphocyte counts and lymphopenia. Further, the obtained CBC testing images used to build an automatic model as a diagnostic system for positive and negative COVID-19 cases. The diagnostic system was achieved 73% for classification accuracy and F-score. Due to endorse the used diagnostic system as a classifier system, we can conclude that the automatic system can be used to train laboratory images of CBC test of COVID-19 patient's datasets with reasonable accuracy before archive them.

Key words : COVID-19, lymphocyte, lymphopenia, azithromycin, hydroxychloroquin, vitamin, image processing, classifier.

How to cite : Qutaiba Mohammed Al Dulaimee, Hanan M. Ali, Saad Shaheen Hammadi and Zainab A. Khalaf (2021) Diagnosis, treatment and classification of COVID-19 disease by complete blood test. *Biochem. Cell. Arch*. **21**, 1211-1216. DocID: https://connectjournals.com/03896.2021.21.1211

INTRODUCTION

The rapid spread of the novel coronavirus (SARS-CoV-2) as a serious threat to the world public health is in dire need of finding potential therapeutic agents (Al-Masoudi *et al*, 2020). Chinese have tested several antiviral and antimalarial drugs as potent inhibitors for the novel virus, such as remdesivir, chloroquine, Hydroxychloroquine, umifenovir and favipiravir. COVID-19 disease is a systemic infection with a significant impact on the hematopoietic system and hemostasis (Terpos *at el*, 2020). Lymphopenia may be considered as a cardinal laboratory finding, with prognostic potential. Neutrophil/lymphocyte ratio and peak platelet/lymphocyte ratio may also have prognostic value in determining severe cases. During the incubation period, usually ranging from 1 to 14 days, and during the early phase of the disease, when non-specific symptoms are present, peripheral blood leukocyte and lymphocyte counts are normal or slightly reduced. Following viremia, SARS-CoV-2 primarily affects the tissues expressing high levels of ACE2 including the lungs, heart, and gastrointestinal tract. Approximately 7 to 14 days from the onset of the initial symptoms, there is a surge in the clinical manifestations of the disease with a pronounced systemic increase of inflammatory mediators and cytokines, which may even be characterized as a "cytokine storm". At this point, significant lymphopenia becomes evident. Although more in-depth research on the underlying etiology is necessary, several factors may contribute to COVID-19 associated lymphopenia. Al Dulaimee *et al* (2020) were observed that the lymphopenia tests should be involved in the diagnosis of COVID-19 disease. They were treated the COVID-19 patient by using a combination of azithromycin (AZM). (500 mg) daily for 6 days, zinc (50 mg) daily for 21 days, hydroxychloroquin (HCQ) caps (400 mg) daily for 10 days, vitamin C (500 mg), vitamin D3 (5000 mg), and doxycycline (100 mg). The results were displayed that the health of each patient was well recovered and all

blood tests were becoming normal after the treatment. Vitamin D deficiency co-exists in patients with COVID-19. At this time, dark skin color, increased age, the presence of pre-existing illnesses and vitamin D deficiency are features of severe COVID-19 disease. Of these, only vitamin D deficiency is modifiable. Through, its interactions with a multitude of cells, vitamin D may have several ways to reduce the risk of acute respiratory tract infections and COVID-19: reducing the survival and replication of viruses, reducing the risk of inflammatory cytokine production, increasing ACE2 concentrations and maintaining endothelial integrity (Mercola *et al*, 2020). During the current corona pandemic, new therapeutic options against this viral disease are urgently desired (Wessels *et al*, 2020). Due to the rapid spread and immense number of affected individuals worldwide, cost-effective, globally available, and safe options with minimal side effects and simple application are extremely warranted.

This paper is organized into two parts: Diagnosis and Treatment and the automatic diagnostic system. The first part is to follow up on the COVID-19 patients requiring treatment in the hospital so that their health improves. In this part, CBC tests are used and then a series of a required drugs are used accordingly. The second part of this paper is to establish a classifier system using deep learning as a diagnostic system for COVID-19 cases.

DIAGNOSIS AND TREATMENT

In this study, all 44 patients were selected randomly from the Rania Hospital, Al Sulaimania, and north of Iraq. These patients were diagnosed with COVID-19 disease, besides low lymphocyte count and lymphopenia, through the complete blood count (CBC). These patients were then treated by using a combination of AZM. (500 mg) daily for 6 days, zinc (20 mg) daily for 21 days, HCQ caps (200 mg) daily for 10 days, and vitamin D3 (5000 Iu). All tests, the white blood cell count (WBC) test, lymphocytes (LYM%) test, LYM test, mid-range cell percentage (MID%) test, mid-range cell (MID) test, granulocyte percentage (GRA%) test, absolute granulocyte (GRA) test, Red Blood Cells Count (RBC) test, Haemoglobin (HGB) test, Haematocrit (HCT) test, Mean Corpuscular Volume (MCV) test, Mean Corpuscular (MCH) test, Mean Corpuscular Haemoglobin Concentration (MCHC) test, Red Cell Distribution Width (RDW%) test, RDWa test, Platelets Count (PLT) test, Mean Platelet Volume (MPV) test, Platelet Distribution Width (PDW) test, Procalcitonin (PCT) test, and Platelet Larger Cell Ratio (LPCR) test, were verified before and after treatment (88, datasets of CBC test images).

RESULTS AND DISCUSSION

The lymphocytes play a decisive role in maintaining immune homeostasis and inflammatory response throughout the body (Tan *et al*, 2020). Understanding the mechanism of compact blood lymphocyte levels is expected to provide an effective strategy for the treatment of COVID-19. Therefore, the association between the COVID-19 symptoms, lymphocyte counts, and lymphopenia needs significant treatment of the dual symptoms in the patients. Owing to, the selected 44 cases from Rania hospital located in Al Sulaimania city in the north of Iraq were diagnosed with COVID-19 disease through symptoms (fever, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, the new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting and diarrhea) and CT scan. The CBC test of each COVID-19 patient was showed low level of lymphocytes cells and lymphopenia. This would serve in providing significant information on the changes that can possibly occur from the CBC of each COVID-19 patient before and after treatment, (WBC, LYM%, LYM, MID%, MID, GRA%, GRAN, RBC, HGB, HCT, MCV, MCH, MCHC, RDW%, RDWa, PLT, MPV, PDW, PCT and LPCR tests). The patients were treated using a combination of AZM. (500 mg) daily for 6 days, zinc (20 mg) daily for 21 days, HCQ caps (200 mg) daily for 10 days and vitamin D3 (5000 Iu). The average results of blood tests before and after treatment (Fig. 1a-t).

Fig. (1a) displays that the results of the WBC test of the infected patients before treatment were seemed to be higher than after treatment. WBC at admission is significantly correlated with death in COVID-19 patients (Feng *et al*, 2020). Higher level of WBC should be given more attention in the treatment of COVID-19. But, Fig. (1b and c) demonstrations different average values of the lymphocyte count and lymphopenia before and after treatment. Lymphopenia can be used as an indicator of disease severity and prognosis of COVID-19 patients (Tan *et al*, 2020). Though, the PLT, MID%, MID, RBC, MCH, MCHC, RDW%, RDWa, PLT, PDW, MPV, PCT and LPCR tests were showed reasonable differs before and after treatment. But, the GRA% and GRAN, Fig. (1g and h) were seeming to remain high in the infected patient rather than the treated one. It has been revealed that lymphocytes express the ACE2 receptor on their surface; thus the SARS-CoV-2 may directly infect those cells and ultimately lead to their lysis (Terpos *at el*, 2020). Furthermore, the cytokine storm is characterized by markedly increased levels of interleukins (mostly IL-6, IL-2, IL-7, granulocyte colony stimulating factor,

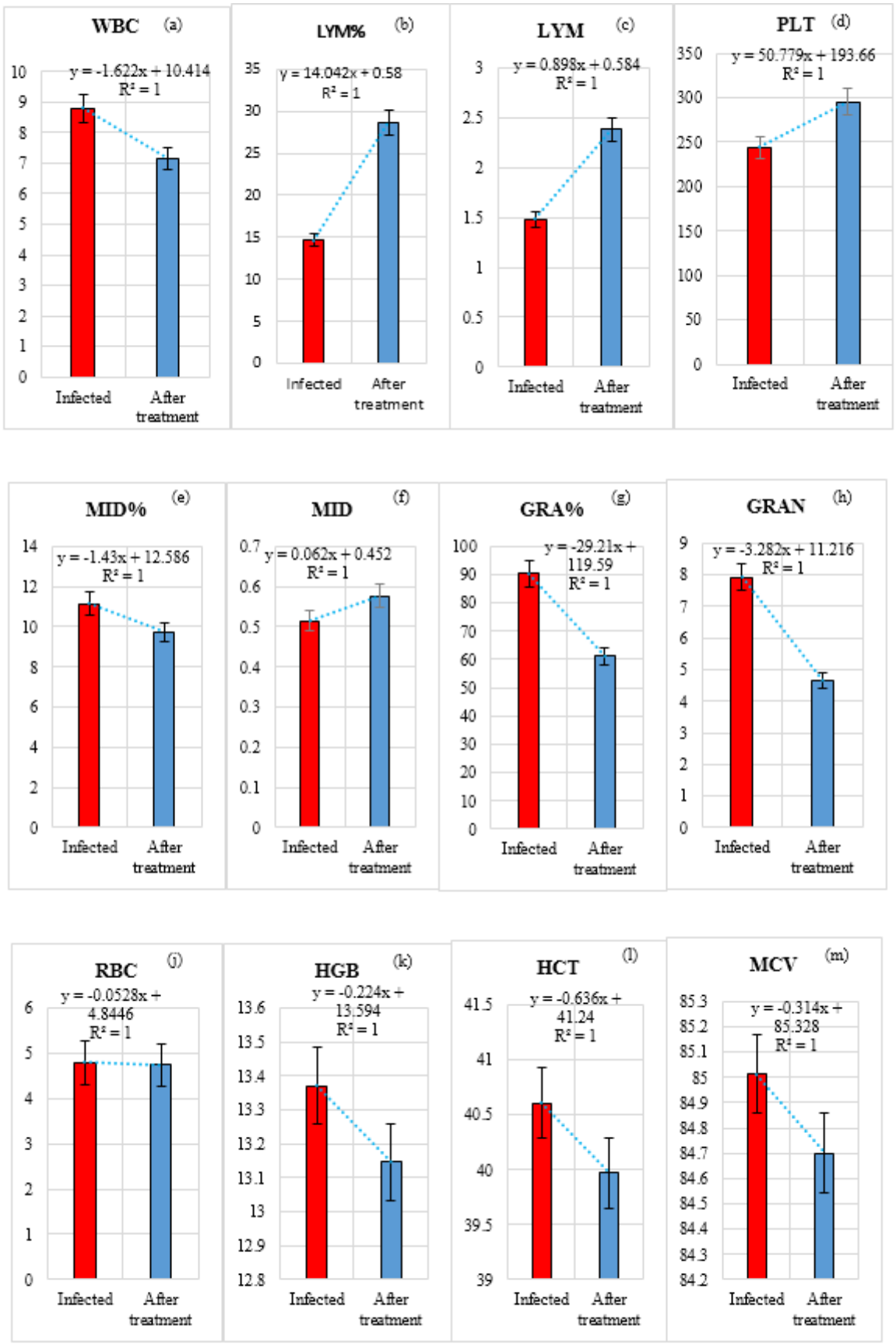
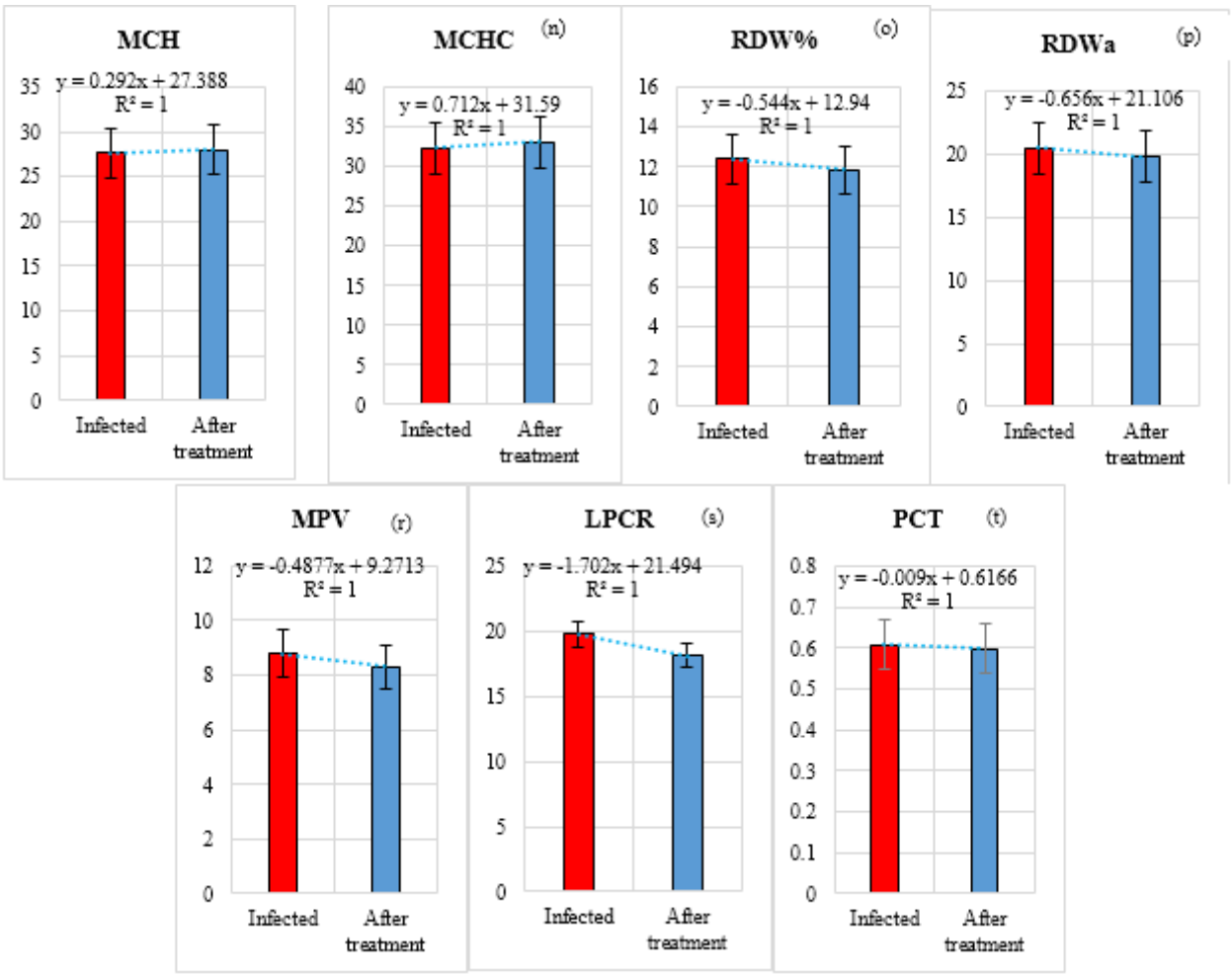


Fig. 1a-t : The average of the results of 44 patients tested before and after treatment.

Fig. 1a-t continued...

Fig. 1a-t continued...



interferon-ã inducible protein 10, MCP-1, MIP1-a) and tumor necrosis factor (TNF)-alpha, which may promote lymphocyte apoptosis. Substantial cytokine activation may be also associated with atrophy of lymphoid organs, including the spleen, and further impairs lymphocyte turnover. Add to which, the HGB, HCT and MCV were also high in the infected patients. They were demonstrated that the CBCs of 208 mild and common COVID-19 cases and the most likely laboratory findings in these patients were abnormalities in RBCs, HGB, HCT and CRP (Djakpo *at el*, 2020). Clinicians should consider these parameters when reading the CBC of COVID-19 patients.

The Automatic diagnostic system

The VGG-16 architecture as a convolutional neural net (CNN) model with many layers was used in this study. The Relu activation function and Softmax were used in hidden layers and in the output layer respectively. Furthermore, the average and the fully connected layers were used. In the deep CNNs, different layers correspond to a hierarchy of features; earlier layers represent more low-level features. Thus, the CNN relevant features were extracted at the highest level (either last convolution or pooling layer) to encode manifestation relationships (Rangarajan *at el*, 2020; Qassim *at el*, 2018).

Evaluation Metric of diagnostic system

Two essential metrics are used to evaluate the classification model performance; these are F1-score and Accuracy. These metrics are measured using a confusion matrix based on four parameters, which are: True positive (TP), which represents the number of patients that are correctly classified. True Negative (TN) is the number of patients that incorrectly assigned to the class. False Positive (FP) is the number of patients that correctly recognized as do not belong to the class, and False Negative (FN) is the number of patients that were not recognized as class cases. That was calculated by the formulas (Sumithra *at el*, 2015):

Accuracy = (TP + TN)\ (TP + FP + TN + FN)

F1-score = (2_Recall_Precision)/(Recall+Precision)

Where,

Precision = TP/ (TP + FP)

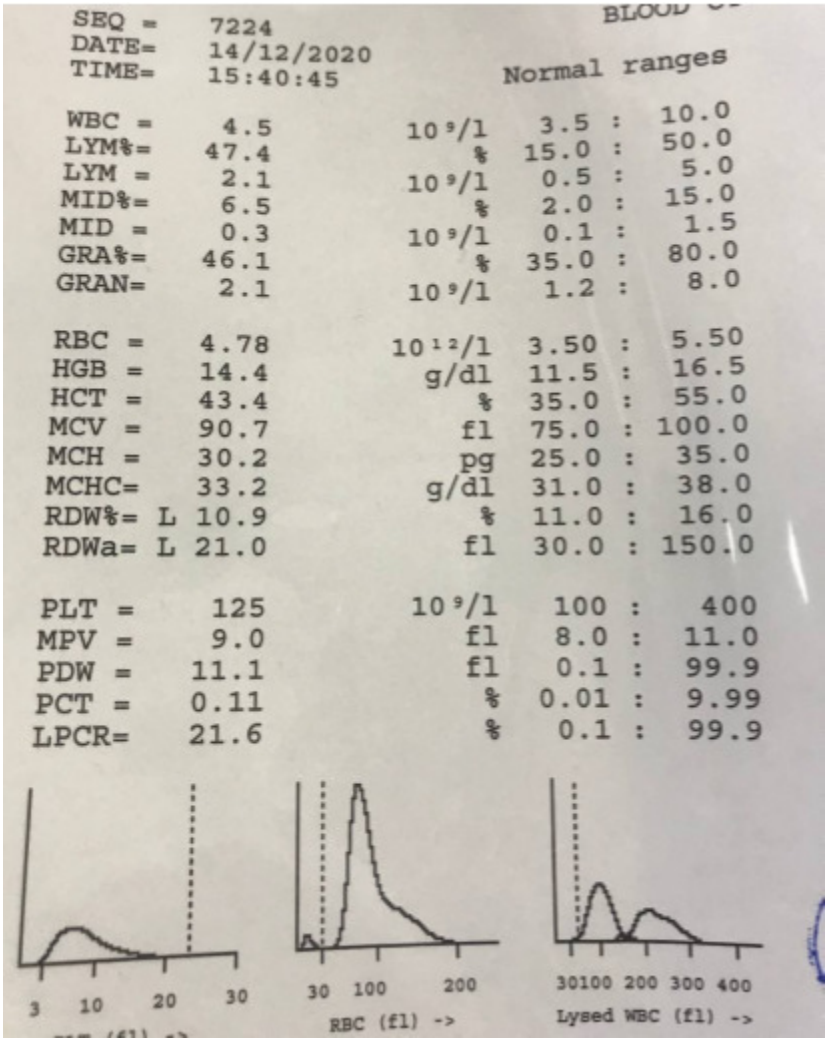


Fig. 2 : Dataset of CBC test image.

Recall = TP/ (FP + FN)

Experiment results of the diagnostic system

The VGG-16 CNN classifier model with the Average Pooling layer that applied in the CNN framework was utilized as a black box deep CNN features extractor. The deep VGG-16 CNN model is trained on CBC test images. Dataset that collected manually form Iraqi patients in Rania Hospital, Al Sulaimania, north of Iraq. These datasets are CBC test images (Fig. 2).

These datasets contain 88 cases that acts each patient before and after treatment. These datasets include of 88 images distributed into two classes, (44 positive cases (infected before treatment) and 44 negative (after treatment)). These images divided into two groups: training and testing. Training data comprised approximately 60 images. While, 24 images were used for testing. Then, the classifier system was produced 73% classification accuracies and F-score.

CONCLUSION

The CBC test may be becoming a significant biomarker for survival patients, that infected with COVID-19. Lymphopenia shows a serious rule in the diagnosis and treatment of COVID-19 disease. The combination of the medicine is the area of research interest. Inexpensive, available, and safe drugs for patients with COVID-19 are very important. Moreover, training CBC test images dataset using deep learning can give significant classification accuracies of CBC test images, which can be used to archive these images obtained from the hospital laboratories or private laboratories.

REFERENCES

Al Dulaimee Q, Ali H and Hammadi S (2020) Combination of Drugs treat COVID-19 patients who are diagnosed with lymphopenia. *Syst. Rev. Pharm.* 1-6.

Al-Masoudi N, Elias R and Saeed B (2020) Molecular docking studies of some antiviral and antimalarial drugs via bindings to 3CLprotease and polymerase enzymes of the novel coronavirus (SARS-CoV-2). *Biointerface Res. Appl. Chem.* **4/10**, 1-14.

Djakpo D K *et al* (2020) Blood routine test in mild and common 2019 coronavirus (COVID-19) patients. *Bioscience Reports* **40**, 1-5.

Feng X, Zhu B, Jiang C, Mi S, Yang L, Zhao Z, Zhang Y and Zhang L (2020) Correlation between White Blood Cell Count at Admission and Mortality in COVID-19 Patients: A Retrospective Study. *BMC Infectious Diseases* 1-10.

Mercola J, Grant W and Wagner C (2020) Review Evidence Regarding Vitamin D and Risk of COVID-19 and Its Severity. *Nutrients* 1-24.

Qassim H, Verma A and Feinzimer D (2018) Compressed residual-VGG16 CNN model for big data places image recognition. In2018 IEEE 8th Annual Computing and Communication Workshop and Conference (CCWC), 169-175. doi: 10.1109/CCWC.2018.8301729.

Rangarajan A K and Purushothaman R (2020) Disease classification in eggplant using pre-trained vgg16 and msvm. *Scientific Reports* **10**, 1-1.

Sumithra R, Suhil M and Guru D S (2015) Segmentation and classification of skin lesions for disease diagnosis. *Procedia Computer Sci.* **45**, 76-85.

Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang Y-Q, Wang Q and Miao H (2020) Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. *Signal Transduction and Targeted Therapy* **5**, 33, doi.org/10.1038/s41392-020-0148-4

Terpos E, Ioannis Ntanasis-Stathopoulos, Ismail Elalamy, Efstathios Kastritis, Theodoros N. Sergentanis, Marianna Politou, Theodora, Psaltopoulou Grigoris, Gerotziafas Meletios and A. Dimopoulos (2020) Hematological findings and complications of COVID-19. *Am. J. Hematol.* **95**, 834-847.

Wessels I, Rolles B and Rink L (2020) The Potential Impact of Zinc Supplementation on COVID-19 Pathogenesis. *Frontiers in Immunology* **11**, 1-11.