

Original Research Article

Evaluation of variations in the various blood indices in COVID recovered patients

Running title: Blood indices in COVID recovered patients

Abstract:

Introduction:

In December 2019, cases of pneumonia with an unknown cause were reported in Wuhan, Hubei Province, China. Novel coronavirus infectious disease (COVID-19) has been spreading worldwide and tracking laboratory indexes during the diagnosis and treatment of patients with severe COVID-19 can provide a reference for patients in other countries and regions. The disease is caused by the Severe Acute Respiratory Syndrome Coronavirus 2 according to studies, and the World Health Organization just dubbed it coronavirus disease 2019.

Comment [DS1]: Non relevant at current time for the purpose of research

Aim: The aim of this analysis ~~was to figure out how~~ is to evaluate COVID-19 patients' blood parameters ~~changed changes and in~~ comparison with healthy controlled patients.

Methods:

Blood samples were taken from 10 patients in which 5 are covid recovered patients and 5 are healthy controls. For these blood samples TBC(Total Blood Count) was taken and the readings of RBC, hemoglobin, WBC, lymphocyte, granulocyte and platelets count was recorded. Independent t-test was done to obtain the results. SPSS software Version 23 was used to give the output comparison as error bar charts.

Comment [DS2]: Too low in view of panademics

Comment [DS3]: ??

Results:

RBC, hemoglobin, WBC, lymphocyte, granulocyte, platelets count was obtained and converted into error bar charts with the help of SPSS 23 software . Mean, Standard deviation, Standard Error mean and p values were obtained . p value are less than 0.005 which is considered to be statistically significant. The results obtained are mentioned in tabular form and represented in graphs.

Comment [DS4]: You have to give an overview about your results
This is description of statistical method only

Conclusion:

From this study ~~we-it~~ can understand that COVID recovered patients have increased RBC count and hemoglobin percentage. The recovered patients have reduced WBC, lymphocytes and Granulocytes percentage. ~~By further studies and more sample size the study can be done in depth thus masking the limitation of the present study.~~

Comment [DS5]: Keep it within text rather than abstract

Keywords: COVID recovered patients, RBC, Hemoglobin, WBC, Lymphocyte, Granulocyte, platelets. Innovative technique.

Introduction

In December 2019, cases of pneumonia with an unknown cause were reported in Wuhan, Hubei Province, China(1),(2). The disease is caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The World Health Organization(WHO) just dubbed it coronavirus disease 2019 (COVID-19) . This novel coronavirus is very infectious and has a long incubation time(3). In the early stages of COVID-19 infection, patients may have symptoms such as fever, dry cough, and exhaustion, but eventually develop acute respiratory distress syndrome (ARDS), respiratory failure, shock, and multiple organ failure, all of which can be fatal(4),(5). The epidemic situation in China has been handled to some extent by a number of preventative control and medical treatment efforts, but cases of illness and mortality outside China have surpassed those in China and are on the rise(3,6). As a result, COVID-19 is a serious worldwide health concern with a high rate of morbidity and mortality.

Lymphocytes are the primary immune cells responsible for viral elimination. The proportion of lymphocytes in peripheral blood normally increases during traditional viral

infections. In severe pandemic H1N1 influenza A and Severe acute respiratory syndrome(SARS), however, peripheral lymphocytopenia was discovered . T cells are important players in adaptive immunity against influenza A virus infection and can help to lessen the severity of symptoms. In patients with influenza A/H1N1 in the acute phase, the total number of lymphocytes, CD3+ T-cells, CD4+ T-cells, and CD8+ T-cells all fell dramatically, according to a study(3,6,7). The National Health Commission of China's seventh edition of the COVID-19 Diagnosis and Treatment Scheme said that a steady reduction in peripheral blood lymphocyte count and a persistent decline in CD4+ T-cells and CD8+ T-cells were signs of a deterioration in the patient's condition(3,6–8).

Although several clinical investigations have identified peripheral lymphocytopenia in COVID-19 patients in laboratory testing, dynamic changes in peripheral blood lymphocyte subsets in COVID-19 patients have been described infrequently. Several biomarkers have been proposed to predict severity and outcomes.(4) However, the predictive role of each markers measurement at presentation, including D-dimer, has not been consistent. (9) Recent studies showed SARS-CoV-2 alters platelet gene expression and activity resulting in platelet hyperreactivity, raising the question of the role of thrombopoiesis in COVID-19(9). Routine complete blood analysis is an inexpensive, widely available and valuable tool which can be used for assessment of the systemic inflammatory response related COVID-19 infection and may help to discriminate between patients with or without severe disease. Mostly RBC will increase as a protective action against the infection and inflammation(8),(10). Post covid usually the test shows the rise of RBC because the oxygen levels will be reduced in the body. The white blood cells (WBC) count of patients with confirmed COVID-19 cases decrease and a definite clinical outcome (death or discharge) may be predicted. The aim of this analysis was to figure out how COVID-19 patients' blood parameters changed and comparison with healthy control individuals.

Materials and Methods

The present cross sectional study was conducted in Saveetha Dental College & Hospitals in AUGUST 2021 and involved normal healthy individuals and patients affected with covid and recovered three months ago. The study and sample collection were approved by the Institutional ethical committee with an approval number of IHEC/SDC/UG-1909/21/241.

Comment [DS6]: Keep it in unified text either covid or COVID or COVID-19 throughout whole text

Patients Selection and Recruitment:

The samples were recruited from the COVID recovered patients. Clinical history was taken from COVID recovered patients. It was also ensured that patients with systemic comorbidities or terminally ill patients were not included for the study. All the patients included in the study belonged to the same ethnic group of Tamil Nadu. Informed consent was obtained from the patients for inclusion in the study and it was also ensured that the patients anonymity was maintained. All the patients completed a questionnaire covering medical, residential, and occupational history.

Comment [DS7]: Like ??? mention and why ?

Variables

Dependent variables was the Hb, RBC, WBC, Lymphocytes, Platelets whereas independent variable was age and sex of the patient.

Comment [DS8]: Units used and reference values

Statistical analysis

The study method used is random controlled sampling. The inclusion criteria is sampling's are Covid recovered and health controls individuals. The exclusion criteria are patients who recovered from Covid more than 3 months and patients with systemic disorders. The dependent variables are age which is 18-20 years and post Covid. Independent variables are gender. The mean values of each parameter were tabulated along with the significant values and plotted in the form of bar graphs using SPSS. Independent t-test analysis was used to compare the results that were obtained.

Results:

The samples were collected from 10 patients in which 5 were covid recovered patients and other 5 were healthy controls. The age of the patients is in the range of 18-20 years old. The patient's blood was collected and a complete blood count test was done and results were analysed.

In the present study, the parameters such as Hb, RBC, WBC, Lymphocytes, Platelets were taken to analyse the changes in the Blood indices in covid recovered patients. The p value of the

parameters were calculated using SPSS software and tabulated (Table-1-6). The independent 't' test values Hb, RBC, WBC, Lymphocytes, Platelets after categorising of COVID recovered patients and healthy controls were compared and depicted in the form of a bar graph (Figure 1-6)

Table 1: Mean and Standard deviation of the WBC count was analyzed.

Comment [DS9]: Units ???

Group	Mean	Standard deviation	Standard Error mean	Sig. P value
Covid recovered	4.2200	.54498	.24372	<0.005
controlled	9.3400	.68411	.30594	

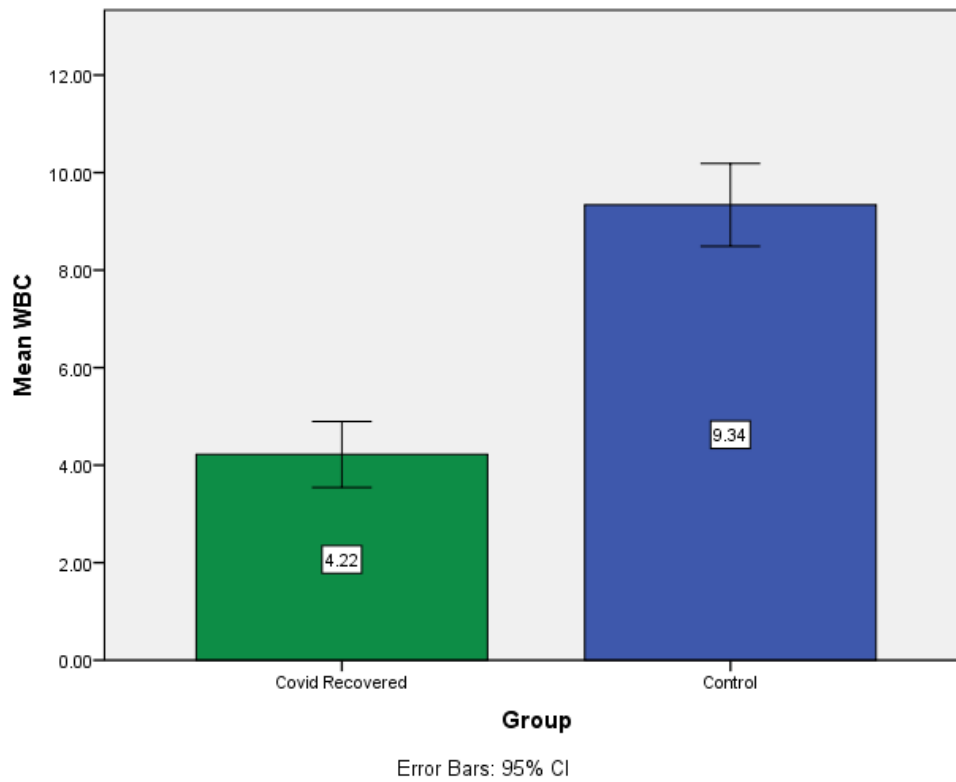


FIGURE 1: Bar graph representing the association between groups with mean WBC. The X-axis represents the group and Y-axis represents the mean WBC. Age group of 18-20 years, the level of control was $9.34 \times 10^3/\mu\text{L}$ (blue) and the level of covid recovered was $4.22 \times 10^3/\mu\text{L}$ (green). P value <0.005.

Table2: Mean and Standard deviation of the RBC count was analyzed.

Group	Mean	Standard deviation	Standard Error mean	Sig. P value
Covid recovered	5.8960	.49707	.22230	<0.005
controlled	4.5660	.39444	.17640	

Comment [DS10]: Units??

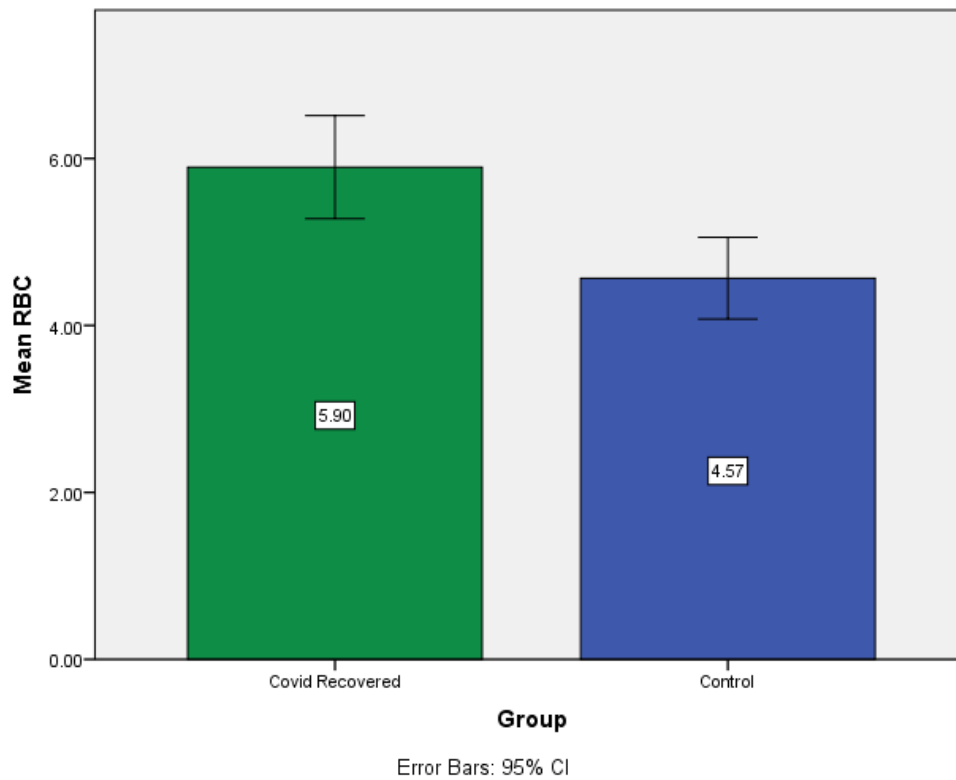


FIGURE 2: Bar graph representing the association between groups with mean RBC. The X-axis represents the group and Y-axis represents the mean RBC. Age group of 18-20 years, the level of control was $4.57 \times 10^6 /\mu\text{L}$ (blue) and level of covid recovered was $5.90 \times 10^6 /\mu\text{L}$ (green). P value <0.005 .

Table3: Mean and Standard deviation of the Lymphocyte count was analyzed.

Comment [DS11]: Units ?

Group	Mean	Standard deviation	Standard Error mean	Sig. P value
Covid recovered	1.6400	.28810	.12884	<0.005
controlled	2.8200	.37683	.16852	

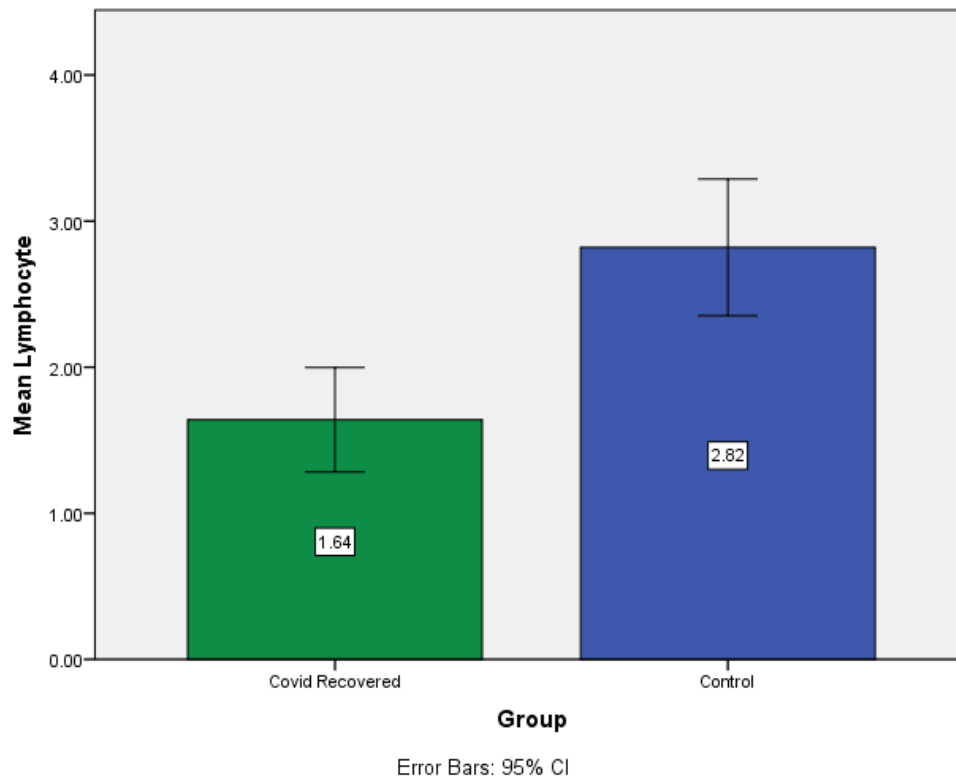


FIGURE 3: Bar graph representing the association between groups with mean Lymphocytes. The X-axis represents the group and Y-axis represents the mean Lymphocyte. Age group of 18-20 years, the level of control was $2.82 \times 10^3/\mu\text{L}$ (blue) and level of covid recovered was $1.64 \times 10^3/\mu\text{L}$ (green). P value <0.005 .

Table 4: Mean and Standard deviation of the Granulocyte count was analyzed.

Group	Mean	Standard deviation	Standard Error mean	Sig. P value
Covid recovered	4.6200	.89833	.40175	>0.005
controlled	6.0800	1.00349	.44878	

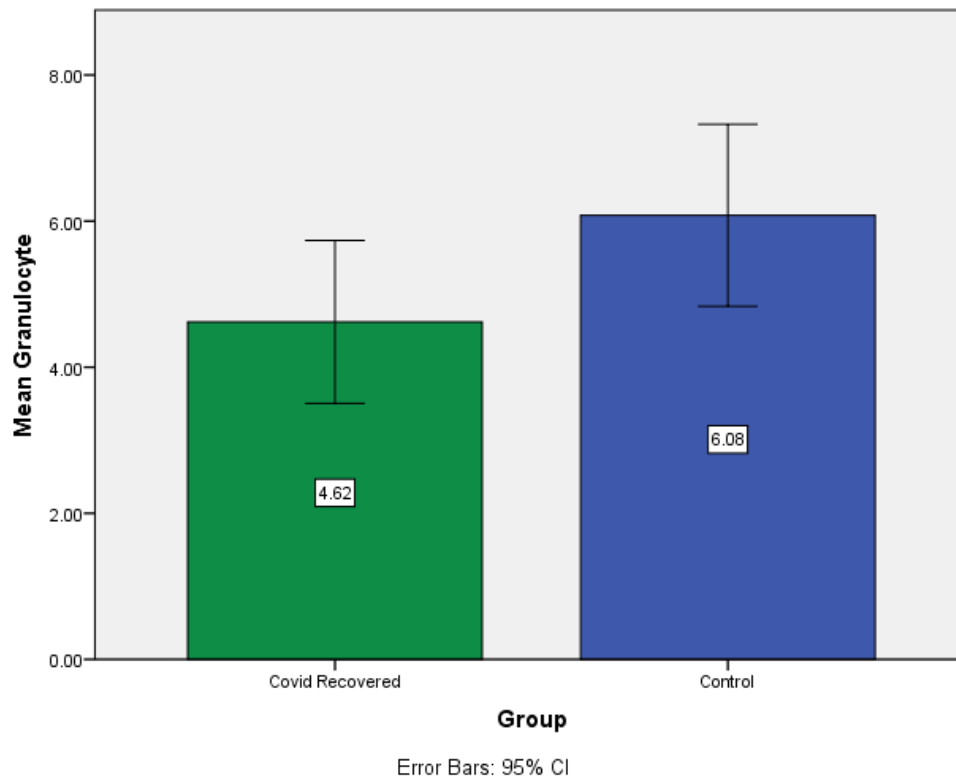


FIGURE 4: Bar graph representing the association between groups with mean Granulocyte. The X-axis represents the group and Y-axis represents the mean Granulocyte. Age group of 18-20 years, the level of control was $6.08 \times 10^3/\mu\text{L}$ (blue) and level of covid recovered was $4.62 \times 10^3/\mu\text{L}$ (green). P value <0.005 .

Table5: Mean and Standard deviation of the Hb count was analyzed.

Group	Mean	Standard deviation	Standard Error mean	Sig. P value
Covid recovered	16.04	.9939	.444	<0.005
controlled	11.8	2.057	.9200	

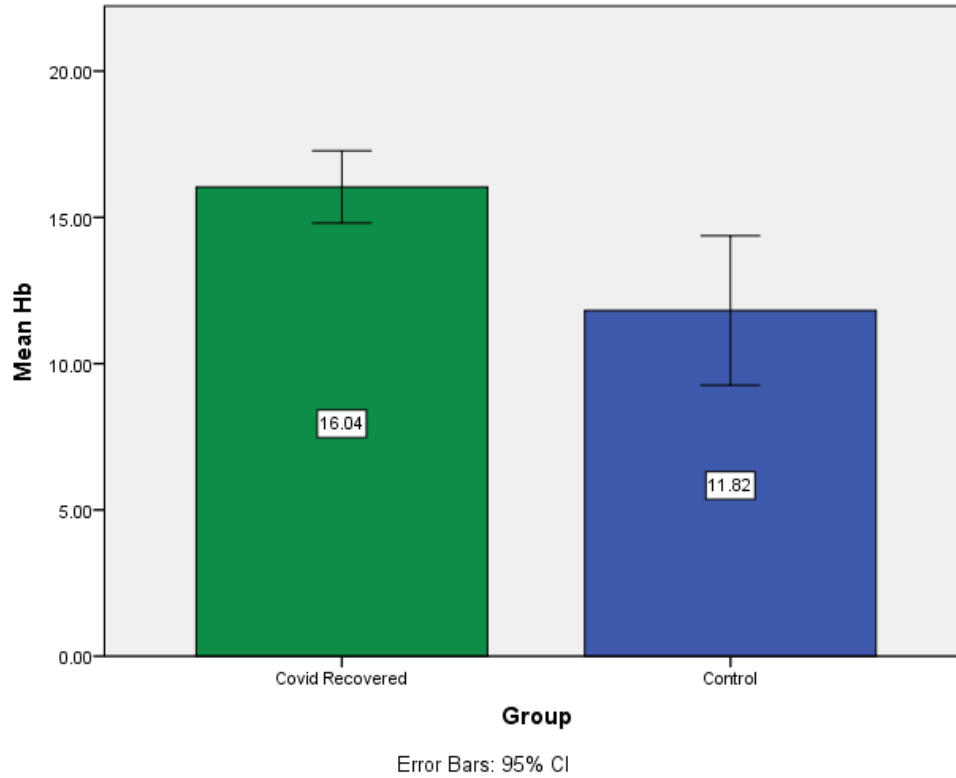


FIGURE 5: Bar graph representing the association between groups with mean Hemoglobin. The X-axis represents the group and Y-axis represents the mean Hemoglobin. Age group of 18-20 years, the level of control was 11.82 g/dl (blue) and level of covid recovered was 16.04 g/dl (green). P value <0.005.

Table6: Mean and Standard deviation of the platelets count was analyzed.

Group	Mean	Standard deviation	Standard Error mean	Sig. P value
Covid recovered	337.2	40.096	17.19	<0.005
controlled	184.2	65.480	29.28	

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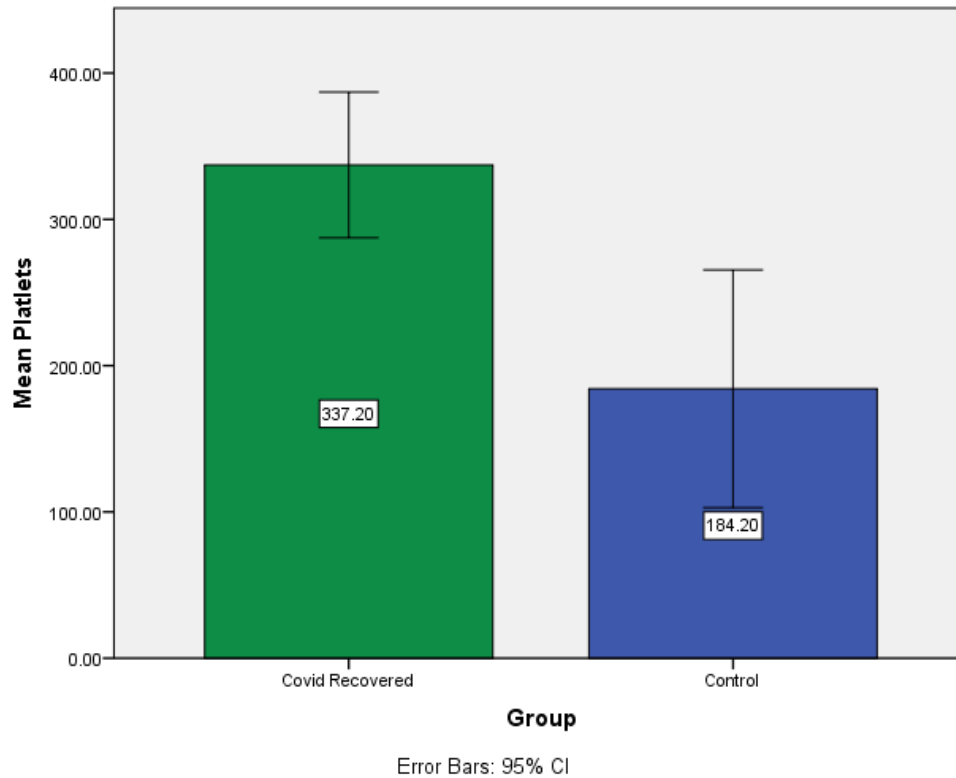


FIGURE 6: Bar graph representing the association between groups with mean Platelet. The X-axis represents the group and Y-axis represents the mean Platelet. In the age group of 18-20 years, the level of control was $184.20 \times 10^3/\mu\text{L}$ (blue) and the level of covid recovered was $337.20 \times 10^3/\mu\text{L}$ (green). P-value <0.005 .

Discussion:

In this study, the comparison of blood indices is done with covid recovered patients and healthy control group in which different parameters were included like Hb, RBC, WBC, Lymphocytes, Platelets (11). Routine blood tests involve analyzing the amount of change and shape distribution in blood cells, such as white blood cells (WBCs), white blood cell categorization count, red blood cell count (RBC), hemoglobin (Hb), and platelets, to assess blood condition and disease. Many pathological changes are detectable by routine blood tests, which can help with diagnosis

when the etiology of the disease is Covid (12). In addition, routine blood tests are a common sign of disease recurrence or recovery, as well as the evaluation of treatment or discontinuance. In the early stages of the disease, the total number of WBCs is normal or decreased, accompanied by decreasing lymphocytes and progressive lymphocytopenia in severe patients.

Lymphocytes, monocytes, and eosinophils all dropped, while total WBC counts were normal. The patient's condition deteriorated, and the total count of WBCs, RBCs, lymphocytes, and granulocytes fell to a low(13). The continuing drop in WBCs was attributed to the virus's direct invasion of hematopoietic cells or the worsening of apoptosis and hematopoietic suppression caused by infection of bone marrow stromal cells(14). Platelet was within the reference range, the trend was similar with WBC too. PLT alterations could be attributed to PLT being an anti-inflammatory factor that increased as a result of recruitment. Furthermore, inflammation and immunological factors boosted thrombopoietin (TPO), which promoted platelet formation. As a result, the pattern was similar to that of neutrophils.

Here it can be understood that in coronavirus infection there will be chronic inflammation and wheezing and trouble in breathing. This leads to a decrease in oxygen levels in the body, to increase the O₂ in the body levels of RBC and hemoglobin are increased in the body. Due to foreign pathogenicity in the body, the body's immune system reacts to it and produces more WBC, lymphocytes, Granulocytes to fight the toxic organisms(15) . Platelets are increased to increase the clotting factors of blood. These all are protective steps taken by the body after recovering from coronavirus. Our team has extensive knowledge and research experience that has translate into high quality publications (16).(17–30) ,(31–35)

The sample size was small and the study was not included with monocyte count and percentage. These were considered as the limitations of our study. In the future, a larger sample size would be used to obtain improved results. Also, with relation to the PLT different other parameters can be taken into account apart from lymphocyte hemoglobin ratio and granulocyte count.

Conclusion:

From the above study, it can be understood that COVID recovered patients have increased RBC count, increased hemoglobin and reduced WBC count with reduced lymphocytes and Granulocytes counts. Here it can be concluded that covid recovered patients

should take care of themselves by having proper care, doctor consultation and follow up. These individuals did not have any serious ailments during the entire duration of the infection and in spite of full recovery, there was significant variation in the blood indices which proves that the after-effects of the viral infection are present even post three months of recovery.

Reference:

1. Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. Addendum: A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020 Dec;588(7836):E6.
2. Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020 Mar;579(7798):270–3.
3. Lachmann G, von Haefen C, Kurth J, Yuerek F, Spies C. Innate immunity recovers earlier than acquired immunity during severe postoperative immunosuppression. *Int J Med Sci*. 2018 Jan 1;15(1):1–9.
4. Lu G, Wang J. Dynamic changes in routine blood parameters of a severe COVID-19 case. *Clin Chim Acta*. 2020 Sep;508:98–102.
5. Li Q, Xu W, Li W, Huang C, Chen L. A 3-Week Dynamic Differences of Immunological Parameters in Severe and Non-severe COVID-19 [Internet]. Available from: <http://dx.doi.org/10.21203/rs.3.rs-36753/v1>
6. Mao J, Dai R, Du R-C, Zhu Y, Shui L-P, Luo X-H. Hematologic changes predict clinical outcome in recovered patients with COVID-19. *Ann Hematol*. 2021 Mar;100(3):675–89.
7. Fu Y-Q, Sun Y-L, Lu S-W, Yang Y, Wang Y, Xu F. Effect of blood analysis and immune function on the prognosis of patients with COVID-19 [Internet]. Vol. 15, *PLOS ONE*. 2020. p. e0240751. Available from: <http://dx.doi.org/10.1371/journal.pone.0240751>
8. Al-Buthabak K, Nafakhi H, Shukur MH, Nafakhi A, Alareedh M, Shaghee F. Blood indices, in-hospital outcome and short-term prognosis in patients with COVID-19 pneumonia. *Monaldi Arch Chest Dis* [Internet]. 2021 Apr 20; Available from: <http://dx.doi.org/10.4081/monaldi.2021.1782>
9. Welder D, Jeon-Slaughter H, Ashraf B, Choi S-H, Chen W, Ibrahim I, et al. Immature platelets as a biomarker for disease severity and mortality in COVID-19 patients. *Br J Haematol*. 2021 Aug;194(3):530–6.
10. Mehta P, Porter JC, Manson JJ, Isaacs JD, Openshaw PJM, McInnes IB, et al. Therapeutic blockade of granulocyte macrophage colony-stimulating factor in COVID-19-associated hyperinflammation: challenges and opportunities. *Lancet Respir Med*. 2020 Aug;8(8):822–

30.

11. Al-Samkari H, Karp Leaf RS, Dzik WH, Carlson JCT, Fogerty AE, Waheed A, et al. COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. *Blood*. 2020 Jul 23;136(4):489–500.
12. He W, Liu X. Significance of peripheral blood indexes in differential diagnoses of SARS-CoV-2 and New Bunia virus. *Sci Rep*. 2021 Jul 8;11(1):14094.
13. Wong CK, Lam CWK, Wu AKL, Ip WK, Lee NLS, Chan IHS, et al. Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome [Internet]. Vol. 136, *Clinical & Experimental Immunology*. 2004. p. 95–103. Available from: <http://dx.doi.org/10.1111/j.1365-2249.2004.02415.x>
14. Saijo M. Severe Fever with Thrombocytopenia Syndrome. *Springer Nature*; 2019. 246 p.
15. Jo Y-S, Kang J-G, Chae J-B, Cho Y-K, Shin J-H, Jheong W-H, et al. Prevalence of Severe Fever with Thrombocytopenia Syndrome Virus in Ticks Collected from National Parks in Korea [Internet]. Vol. 19, *Vector-Borne and Zoonotic Diseases*. 2019. p. 284–9. Available from: <http://dx.doi.org/10.1089/vbz.2018.2338>
16. Anita R, Paramasivam A, Priyadharsini JV, Chitra S. The m6A readers and aberrations associated with metastasis and predict poor prognosis in breast cancer patients. *Am J Cancer Res*. 2020 Aug 1;10(8):2546–54.
17. Jayaseelan VP, Paramasivam A. Emerging role of NET inhibitors in cardiovascular diseases. *Hypertens Res*. 2020 Dec;43(12):1459–61.
18. Sivakumar S, Smiline Girija AS, Vijayashree Priyadharsini J. Evaluation of the inhibitory effect of caffeic acid and gallic acid on tetR and tetM efflux pumps mediating tetracycline resistance in *Streptococcus* sp., using computational approach. *Journal of King Saud University - Science*. 2020 Jan 1;32(1):904–9.
19. Smiline Girija AS. Delineating the Immuno-Dominant Antigenic Vaccine Peptides Against gacS-Sensor Kinase in *Acinetobacter baumannii*: An in silico Investigational Approach. *Front Microbiol*. 2020 Sep 8;11:2078.
20. Iswarya Jaisankar A, Smiline Girija AS, Gunasekaran S, Vijayashree Priyadharsini J. Molecular characterisation of csgA gene among ESBL strains of *A. baumannii* and targeting with essential oil compounds from *Azadirachta indica*. *Journal of King Saud University - Science*. 2020 Dec 1;32(8):3380–7.
21. Girija ASS. Fox3+ CD25+ CD4+ T-regulatory cells may transform the nCoV's final destiny to CNS! *J Med Virol* [Internet]. 2020 Sep 3; Available from: <http://dx.doi.org/10.1002/jmv.26482>
22. Jayaseelan VP, Ramesh A, Arumugam P. Breast cancer and DDT: putative interactions, associated gene alterations, and molecular pathways. *Environ Sci Pollut Res Int*. 2021

Jun;28(21):27162–73.

23. Arumugam P, George R, Jayaseelan VP. Aberrations of m6A regulators are associated with tumorigenesis and metastasis in head and neck squamous cell carcinoma. *Arch Oral Biol*. 2021 Feb;122:105030.
24. Kumar SP, Girija ASS, Priyadharsini JV. Targeting NM23-H1-mediated inhibition of tumour metastasis in viral hepatitis with bioactive compounds from *Ganoderma lucidum*: A computational study. *pharmaceutical-sciences* [Internet]. 2020;82(2). Available from: <https://www.ijpsonline.com/articles/targeting-nm23h1-mediated-inhibition-of-tumour-metastasis-in-viral-hepatitis-with-bioactive-compounds-from-ganoderma-lucidum-a-comp-3883.html>
25. Girija SA, Priyadharsini JV, Paramasivam A. Prevalence of carbapenem-hydrolyzing OXA-type β -lactamases among *Acinetobacter baumannii* in patients with severe urinary tract infection. *Acta Microbiol Immunol Hung*. 2019 Dec 9;67(1):49–55.
26. Priyadharsini JV, Paramasivam A. RNA editors: key regulators of viral response in cancer patients. *Epigenomics*. 2021 Feb;13(3):165–7.
27. Mathivadani V, Smiline AS, Priyadharsini JV. Targeting Epstein-Barr virus nuclear antigen 1 (EBNA-1) with *Murraya koengii* bio-compounds: An in-silico approach. *Acta Virol*. 2020;64(1):93–9.
28. Girija As S, Priyadharsini J V, A P. Prevalence of Acb and non-Acb complex in elderly population with urinary tract infection (UTI). *Acta Clin Belg*. 2021 Apr;76(2):106–12.
29. Anchana SR, Girija SAS, Gunasekaran S, Priyadharsini VJ. Detection of *csgA* gene in carbapenem-resistant *Acinetobacter baumannii* strains and targeting with *Ocimum sanctum* biocompounds. *Iran J Basic Med Sci*. 2021 May;24(5):690–8.
30. Girija ASS, Shoba G, Priyadharsini JV. Accessing the T-Cell and B-Cell Immuno-Dominant Peptides from *A.baumannii* Biofilm Associated Protein (bap) as Vaccine Candidates: A Computational Approach. *Int J Pept Res Ther*. 2021 Mar 1;27(1):37–45.
31. Arvind P TR, Jain RK. Skeletally anchored forsus fatigue resistant device for correction of Class II malocclusions-A systematic review and meta-analysis. *Orthod Craniofac Res*. 2021 Feb;24(1):52–61.
32. Venugopal A, Vaid N, Bowman SJ. Outstanding, yet redundant? After all, you may be another *Cholutedca Bridge!* *Semin Orthod*. 2021 Mar 1;27(1):53–6.
33. Ramadurai N, Gurunathan D, Samuel AV, Subramanian E, Rodrigues SJL. Effectiveness of 2% Articaine as an anesthetic agent in children: randomized controlled trial. *Clin Oral Investig*. 2019 Sep;23(9):3543–50.
34. Varghese SS, Ramesh A, Veeraiyan DN. Blended Module-Based Teaching in Biostatistics and Research Methodology: A Retrospective Study with Postgraduate Dental Students. *J*

Dent Educ. 2019 Apr;83(4):445–50.

35. Mathew MG, Samuel SR, Soni AJ, Roopa KB. Evaluation of adhesion of *Streptococcus mutans*, plaque accumulation on zirconia and stainless steel crowns, and surrounding gingival inflammation in primary molars: randomized controlled trial [Internet]. Vol. 24, *Clinical Oral Investigations*. 2020. p. 3275–80. Available from: <http://dx.doi.org/10.1007/s00784-020-03204-9>

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