

Dynamics of COVID-19 Lockdown on Blood Indices and Its Impact on Individuals' Immunological Health Status: A Cohort Study in Madinah, Saudi Arabia

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Objective: The complete blood count (CBC) is an essential blood test that has been used for decades to assess individuals' overall health status. This study aimed to investigate the contributions of lockdown conditions to individuals' overall health status using blood indices as biological markers. During lockdown, people are limited to confined spaces, have access to limited nutritional supply options, experience increased stress, and are exposed to other environmental factors.

Methods: Our study's target population included all outpatients who were severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-negative and requested CBC assessments as part of their routine health checks. A total of 2414 CBC results were included, covering a period from February 2019 to December 2020. The average of different blood indices during the COVID-19 lockdown was compared to the 10-month period preceding the lockdown.

Results: The average counts of RBCs, hemoglobin, and hematocrit showed a significant increase during the lockdown period, which lasted from May 2020 to September 2020. Reductions were observed for the RBC distribution width, total white blood cell count, platelets, and platelet distribution width.

Conclusion: Our findings suggested that the overall health status of individuals improved during the lockdown period in the short term, but health status might be adversely affected under these conditions of a longer period. Both RDW and PDW could be used as indicators for the overall health status when assessed against other blood indices.

Keywords: COVID-19, CBC, lockdown, platelet distribution width, red cell distribution width

Introduction

The complete blood count (CBC) has been used for decades as an essential blood test to assess individuals' overall health status.¹ Specific blood indices, such as the total count of red blood cells (RBCs) which is important to understand the production capacity of the bone marrow, mean corpuscular volume (MCV) which reflects the cell's size, mean corpuscular hemoglobin (MCH), cell distribution width (RDW) which represent the variation in size between different RBCs, and hemoglobin concentration (HGB) which is used to monitor the blood's oxygenation capacity, have a significant diagnostic value in reflecting bone marrow's ability to produce hematopoietic-driven cells.^{2,3} Other

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indices related to white blood cells (WBC) and the differential count of each one of them had been used as markers for inflammatory reactions such as bacterial infections, viral infections, parasitic infections, or hematological malignancies.^{4,5}

The immune system is composed of many intertwined cells and organs working in harmony to create the overall protection against pathogens. White blood cell count is very important indicator of how the immune system handles certain clinical and medical situations such as inflammatory reactions or infections by foreign organisms.^{6–9}

SARS-CoV-2 is a single-strand RNA virus belonging to the Coronaviridae family of viruses. It is the primary cause of respiratory symptoms worldwide since the outbreak in Wuhan in January 2020.¹⁰ Viral infections are represented in the blood work as a marked increase in total WBC count underlying a significant surge in lymphocytes, which are produced by the immune system as an antiviral response driven by interferons.^{11–13}

The balance in different whole blood indices is essential to maintain the equilibrium of many important blood components such as albumin and plasma proteins. That is why a CBC is ordered and considered an essential blood test in the first line of the diagnostic process in many clinical complications.¹⁴

In this study, we aim to investigate the role of COVID-19 and the accompanying lockdown that was enforced between May 2020 and September 2020 on patients' blood indices in Medina region. We ask if these indices can be used to measure the overall health status of individuals and if a significant difference in blood indices is noticed that may be attributed directly to certain lifestyle changes associated with the lockdown.

Materials and Methods

Ethics Statement

This study was approved by the Internal Review Board of Taibah University in Madinah, Saudi Arabia (No. 2021/90/114/MLT). Written informed consent was obtained from each patient prior to participation in the study.

Study Population

Our study's target population were all out-patients who were SARS-CoV-2 negative and requested a complete blood count (CBC). Any patient showing respiratory symptoms or was less than 18 years were excluded from the study. A total of 2414 CBC results were obtained from

Table 1 Target Population Used for This Study (n = 2414)

Gender	Male	Female
Max Age	91	82
Min Age	18	18
Average Age	27	29
Count	772	1642

the laboratory information system (Table 1). These results were from 772 males (aged between 18 and 91 years) and 1642 females (aged between 18 and 82 years).

Complete Blood Count

Three milliliters of whole blood samples were collected in Lavender top tubes containing EDTA K3 (Advanced Medical Co., Riyadh) and then placed on a roller (12 RPM) until the analysis. CBC analysis was performed between 10 minutes and 3 hours after sample collection on the XP-300 Automated Hematology Analyzer (Sysmex Corporation, Hyogo).

Statistical Analysis

Blood indices were accumulated for each month to calculate the average, SD, and SEM and then blotted as graphical reorientations. Significance in the difference between monthly averages was calculated using the 2-sample *t*-test, which is commonly used to compare two independent parametric groups and tests the null hypothesis, assuming that both means are identical.¹⁵ Additionally, the Violin plot was used to compare the averages of the entire time periods. The unpaired *t*-test, and the *F*-test were performed to calculate the *p*-value. Statistical analysis and graphical representation of data were performed using Prism 8.2 (GraphPad Software, Inc., San Diego).

Results

Iron-Related CBC Indices are Increased During the Lockdown Period

For the 10 months preceding the lockdown, the average RBC count was $4.32 \times 10^6/\mu\text{L}$ (Figure 1). This average showed a significant increase to $4.59 \times 10^6/\mu\text{L}$, an approximate 7% increase (Figure 2), for the lockdown period, which started in May 2019 and lasted for 5 months. This increase was determined to be significant using both the unpaired *t*-test and the *F*-test with a *p*-value of <0.0001 in both statistical tests. This observation was not limited to only RBCs. We showed that Hemoglobin and Hematocrit (Figure 1) showed

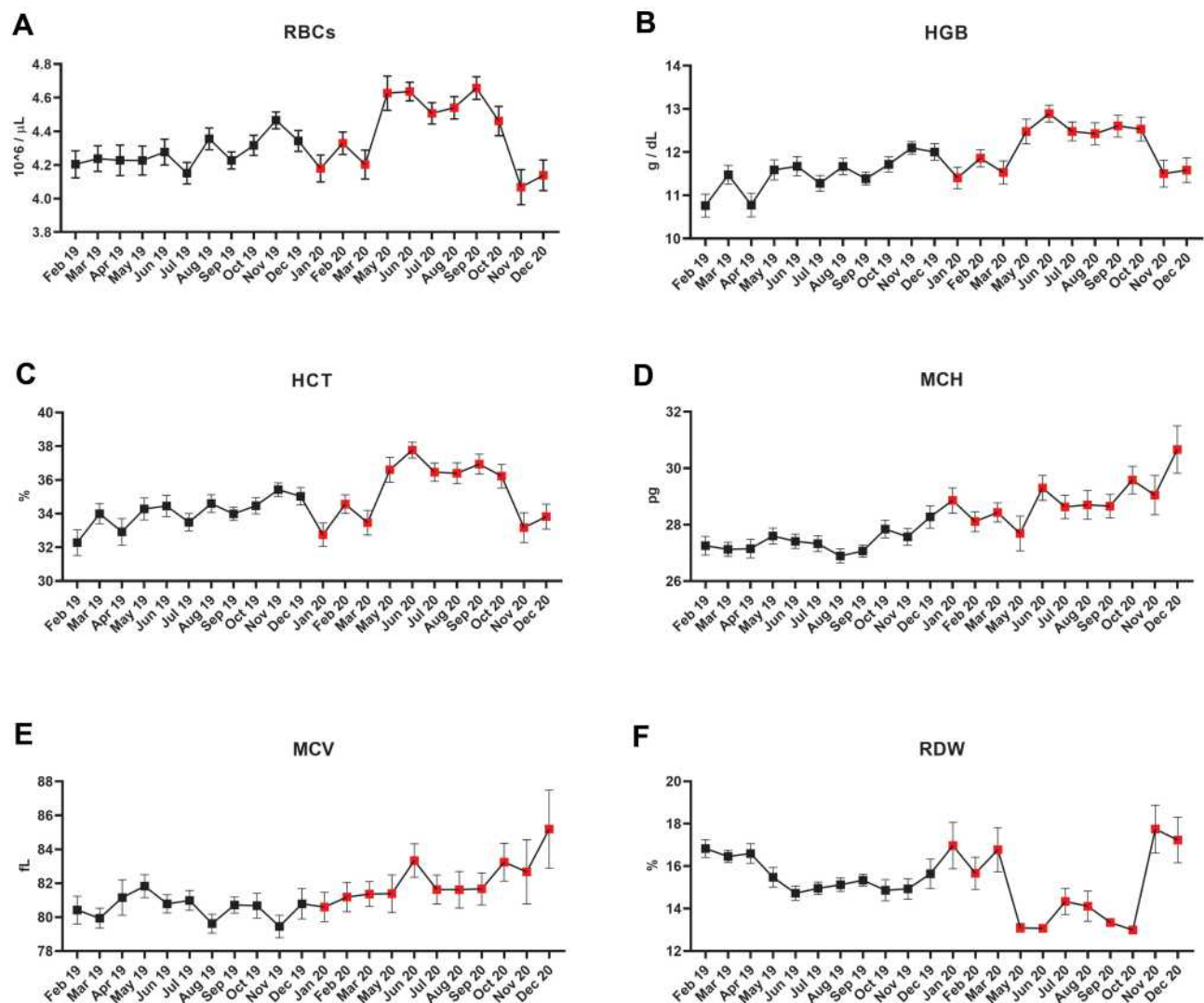


Figure 1 Accumulative representation of RBC-related blood indices for 2414 patients shown in months from February 2019 until December 2020. (A) Red blood cells (RBC) counts are shown as average for each month $\pm$ SEM in $10^6/\mu\text{L}$; (B) Hemoglobin levels are shown as average for each month $\pm$ SEM in g/dL; (C) Hematocrit levels are shown as average for each month $\pm$ SEM in percentage; (D) Mean corpuscular hemoglobin (MCH) levels are shown as average for each month $\pm$ SEM in pg; (E) Mean corpuscular volume (MCV) levels are shown as average for each month $\pm$ SEM in fL; (F) RBC distribution width (RDW) levels are shown as average for each month $\pm$ SEM in percentage.

very similar results as RBCs (Table 2). Hemoglobin concentration increased significantly from 11.69 g/dL to 12.61 g/dL ($t=7.511$; $p\text{-value} < 0.0001$), as well as Hematocrit which increased significantly from 34.33% to 36.91% ($t=7.876$; $p\text{-value} < 0.001$; $F=1.223$; $p\text{-value} < 0.01$). This clearly indicates that iron-related CBC indices are increased during the lockdown when compared to before that time period (Figure 2). RBC mean corpuscular volumes as well as corpuscular hemoglobin concentrations did not show any significant difference between the two time periods. The MCV average remained steady at 80.3 fL as well as the MCH average at 27.4 pg. The RBC distribution width (RDW-CV), on the other hand, showed a marked decrease from 15.27%

to 14.40% in the lockdown period ($t=3.988$; $p\text{-value} < 0.001$; $F=1.662$; $p\text{-value} < 0.01$).

White Blood Cell Counts are Decreased During the Lockdown Period

We then compared total WBC counts and the percentage of neutrophil and lymphocyte to the total counts (Figure 3). Total WBC was significantly lower during the lockdown period than in the previous 10 months (Table 3). The average WBC count before the lockdown was $8.423 \times 10^3/\mu\text{L}$ which dropped to $7.156 \times 10^3/\mu\text{L}$ during the lockdown. This decrease was determined to be statistically significant ($t=5.581$; $p\text{-value} < 0.001$; $F=3.841$; $p\text{-value} < 0.001$). However, lymphocyte

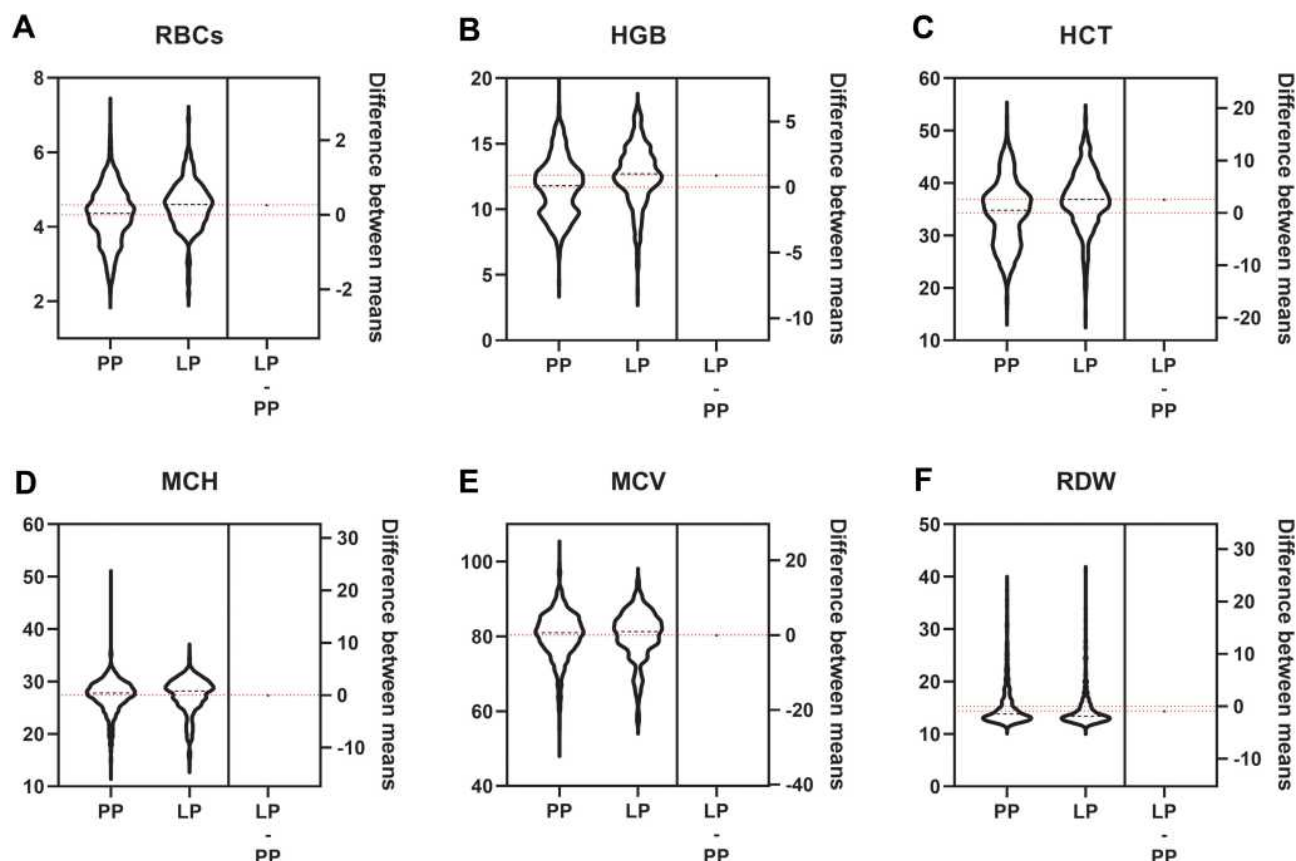


Figure 2 Difference between average means of blood indices. (A) RBCs: red blood cells. (B) HGB: hemoglobin. (C) HCT: hematocrit. (D) MCH: mean corpuscular hemoglobin. (E) MCV: mean corpuscular volume. (F) RDW: RBC distribution width.

Abbreviations: PP, period preceding the lockdown; LP, lockdown period.

and neutrophil counts remained on a relatively steady average (Table 3) throughout the year (Figure 4).

Platelet Counts are Decreased During the Lockdown Period

After that, we looked at Platelet counts, which showed a similar drop during the lockdown (Figure 5). Platelet

counts showed an average of $361 \times 10^3/\mu\text{L}$ before the lockdown (Table 4). This average was significantly lowered to $318 \times 10^3/\mu\text{L}$ ($t = 4.659$; $p\text{-value} = <0.001$; $F = 2.732$; $p\text{-value} = <0.001$). More interestingly, the Platelet distribution width (PDW) was also lowered (Figure 6) from 13.18% to 12.58% ($t = 4.439$; $p\text{-value} = <0.001$; $F = 1.700$; $p\text{-value} = <0.001$).

Table 2 Statistical Analysis for Average Counts of RBC-Related Indices

Parameter	Mean PP	Mean LP	95% Confidence Interval	Unpaired t Test			F-Test		
				p-value	t	df	p-value	F	DFn
RBC	4.32	4.59	0.1936 to 0.3500	<0.001	6.817	1615	<0.001	1.359	1183
HGB	11.69	12.61	0.6781 to 1.157	<0.001	7.511	1715	NS	1.044	440
HCT	34.33	36.91	1.940 to 3.227	<0.001	7.876	1722	<0.01	1.223	1279
MCH	27.38	27.44	-0.2725 to 0.4048	NS	0.383	1704	NS	1.184	437
MCV	80.35	80.39	-0.6482 to 0.7249	NS	0.109	1709	NS	1.070	441
RDW	15.27	14.40	-1.301 to -0.4431	<0.001	3.988	1703	<0.001	1.662	1265

Notes: Comparison was performed between the "Lockdown Period: LP" which lasted for five months (from May 2020 until September 2020), and the "Preceding Period: PP" which lasted for 10 months (from July 2019 until April 2020). Mean: average value of all data in that particular time period.

Abbreviation: NS, not significant.

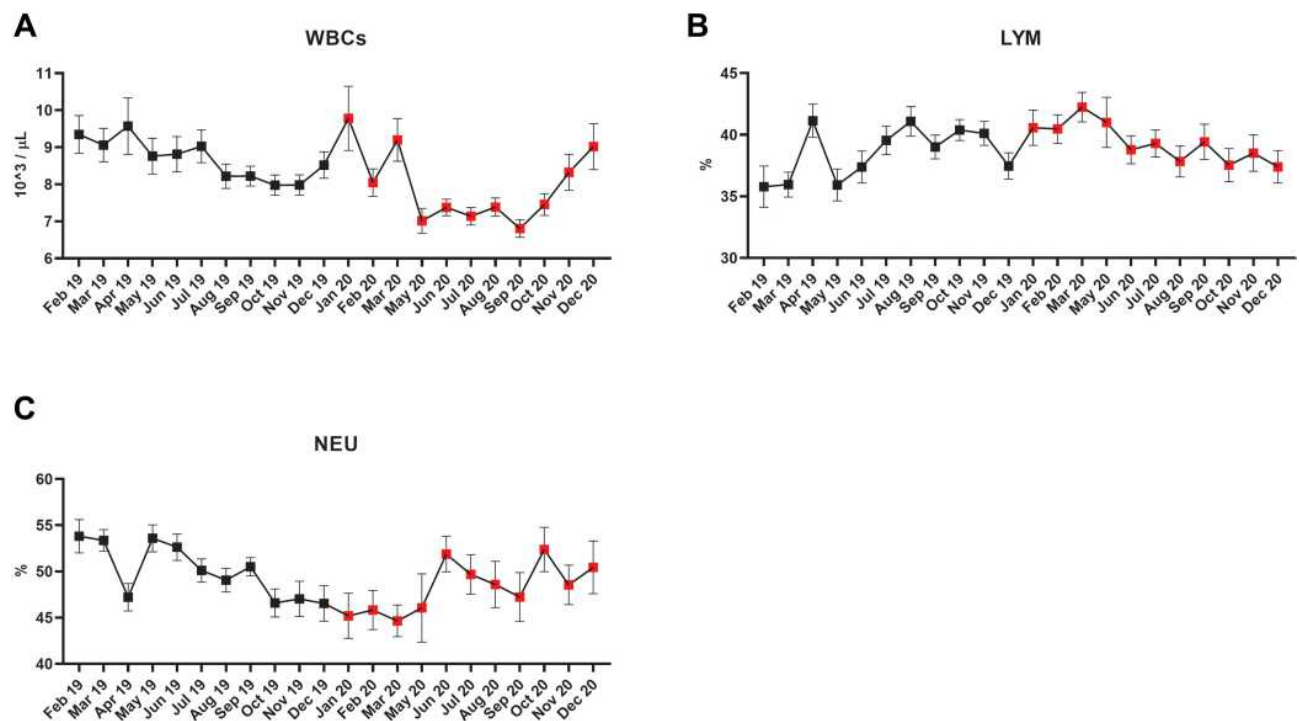


Figure 3 Accumulative representation of WBC-related blood indices for 2414 patients shown in months from February 2019 until December 2020. **(A)** Total white blood cells (WBC) counts are shown as average for each month $\pm$ SEM in $10^3/\mu\text{L}$; **(B)** Lymphocyte percentages are shown as average for each month $\pm$ SEM in percentage; **(C)** Neutrophil percentages levels are shown as average for each month $\pm$ SEM in percentage.

Discussion

Many factors are involved in regulating the cellular composition in our blood. These factors come from the environment we share, the food we eat, the atmosphere we breathe, and the pathogens transmitted between individuals in a particular community. The Corona pandemic showed us that many elements are still hidden from our understanding of our bodies' essential biological functions. One of the immune system's primary clinical facts is the noticeable increase of cellular and humoral factors upon acquiring an infection. SARS-CoV-2, such as any pathogen, should show similar effects on the parameters of our immune system. However, a question arises about the

people who were not infected with the virus or those who have recovered (for more than 30 days or more).

Our study aimed to understand the overall individuals' immunological status during the lockdown period in Madinah, Saudi Arabia, which lasted for about 5 months, starting from April 2020 until September 2020. People in lockdown practice their daily routines in an entirely different extent than their regular routine which can be clearly observed from our results. Basic daily routines such as physical activity, smoking frequency, type and quantity of food, mental and physiological stress are just a few factors shaping how our body reacts to the external environment.

Table 3 Statistical Analysis for Average Counts of WBC-Related Indices

Parameter	Mean PP	Mean LP	95% Confidence Interval	Unpaired t Test			F Test		
				p-value	t	df	p-value	F	DFn
WBC	8.423	7.156	-1.712 to -0.8216	<0.001	5.581	1718	<0.001	3.841	1277
LYM	39.98	39.15	-2.217 to 0.5505	NS	1.181	1703	NS	1.110	1266
NEU	50.03	50.91	0.4100 to 3.350	NS	2.508	1702	NS	1.079	1265

Notes: Comparison was performed between the "Lockdown Period: LP", which lasted for 5 months (from May 2020 until September 2020), and the "Preceding Period: PP" which lasted for 10 months (from July 2019 until April 2020). Mean: average value of all data in that particular time period.

Abbreviation: NS, not significant.

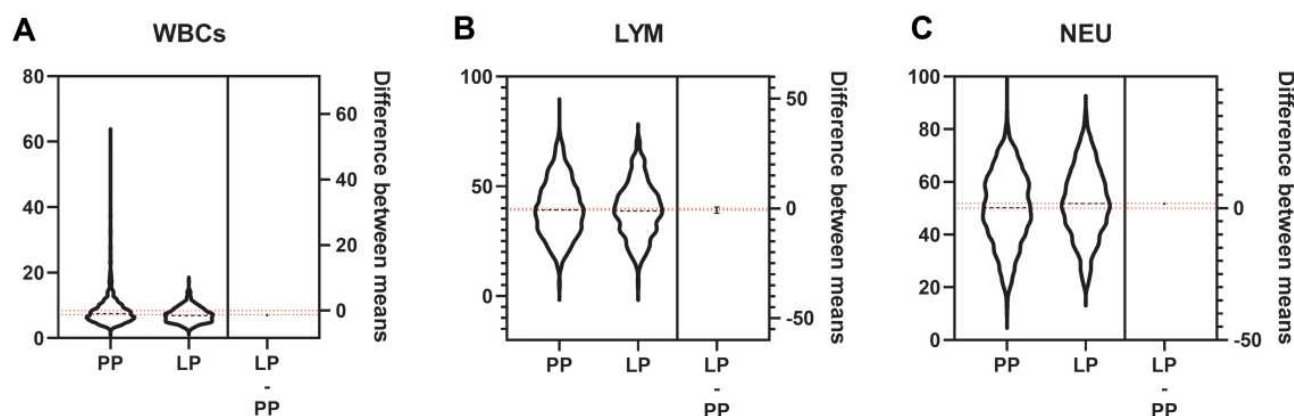


Figure 4 Difference between average means of blood indices. **(A)** WBCs: white blood cells. **(B)** LYM: lymphocytes. **(C)** NEU: neutrophils. **Abbreviations:** PP, period preceding the lockdown; LP, lockdown period.

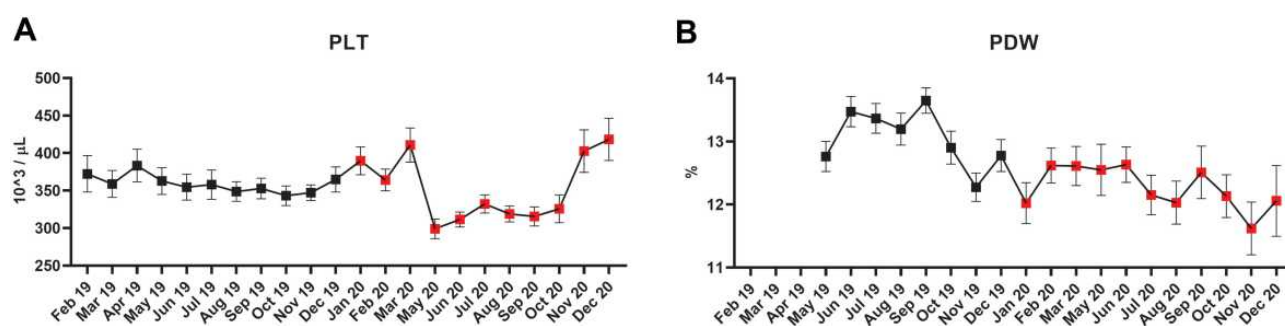


Figure 5 Accumulative representation of platelet-related blood indices for 2414 patients shown in months from February 2019 until December 2020. **(A)** Platelet counts are shown as average for each month $\pm$ SEM in $10^6/\mu\text{L}$; **(B)** Platelet distribution width (PDW) levels are shown as average for each month $\pm$ SEM in percentage.

Here we show that RBC counts along with hemoglobin and hematocrit levels showed a significant increase in our target population during the lockdown period. This increase can be attributed to many factors, most notably smoking. Tobacco smoking is directly linked to an increase in RBC counts and related indices. More importantly, many published studies showed that smoking routine increased considerably among people during the lockdown as a coping mechanism against physical and mental stress.¹⁶ Interestingly, the moving average of both

MCV and MCH showed no significant deviation throughout the year. This was in agreement with previously published studies showing that smoking had no significant effect on those two hematological parameters.^{17,18}

Moreover, RDW rates were lower during the lockdown period than before the lockdown. RDW represents the uniformity of RBC size, where lower percentages mean that all cells are almost the same size.¹⁹ This uniformity in size may indicate that the overall oxygenation requirement levels of those individuals are remarkably similar. Also,

Table 4 Statistical Analysis for Average Counts of Platelet-Related Indices

Parameter	Mean PP	Mean LP	95% Confidence Interval	Unpaired t Test			F Test		
				p-value	t	df	p-value	F	DFn
PLT	361.7	318.2	-61.80 to -25.18	<0.001	4.659	1703	<0.001	2.732	1266
PDW	13.18	12.58	-0.8642 to -0.3345	<0.001	4.439	1587	<0.001	1.700	1167

Notes: Comparison was performed between the "Lockdown Period: LP", which lasted for 5 months (from May 2020 until September 2020), and the "Preceding Period: PP", which lasted for 10 months (from July 2019 until April 2020). Mean: average value of all data in that particular time period.

Abbreviation: NS, not significant.

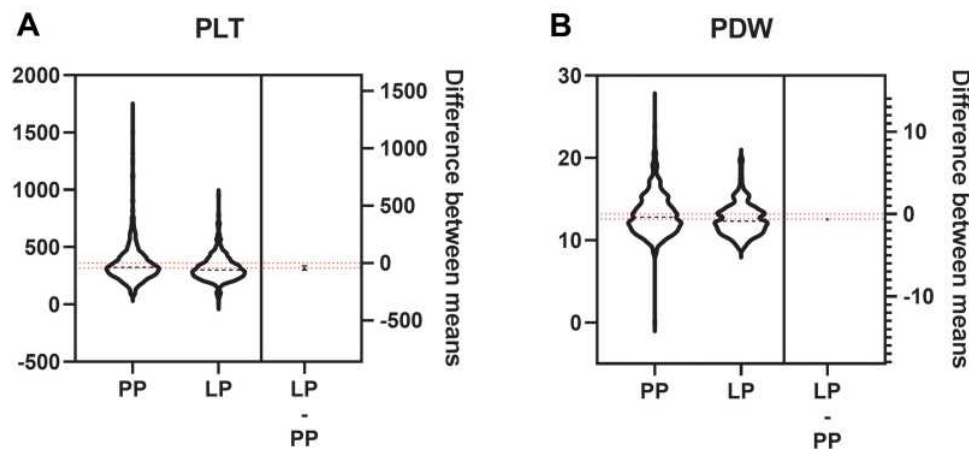


Figure 6 Difference between average means of blood indices. **(A)** PLT: platelets. **(B)** PDW: platelet distribution width.
Abbreviations: PP, period preceding the lockdown; LP, lockdown period.

many researchers have proposed the use of high RDW as a pathological marker in many disease models.^{20–25} RDW is an actual representation of volumetric differences between many red blood cell populations including mature red cells, immature red cells and retics. The same technological concept applies to PDW in the context of platelets. Lower RDW might therefore indicate a healthy status, or in other terms, the absence of these pathological conditions. This finding also contradicts the notion of smoking as a detrimental factor of the high levels of RBC, HGB, and HCT.

Immunological status of individuals is very hard to assess. Many biological factors must be considered, such as a healthy diet, physical exercise, proper adherence to medical management, and other factors. The collection of blood specimens from different individuals before and during the lockdown would also generate some statistical bias that needs to be taken into consideration. Recent studies from Saudi Arabia showed that compliance with the medicinal regiment and following a healthy dietary routine were both diminished during the lockdown period.^{26,27} Our results may shed some light on the impact of reduced physical activity accompanied with high mental stress on individuals' immune systems by using blood indices as a supporting factor.

Disclosure

The author reported no conflicts of interest for this work.

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