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# **Complete Blood Count (CBC) and Multivariate Analysis as Tools for Predicting Coronavirus (COVID-19) Infectious**

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#### **Abstract**

The COVID-19 pandemic has affected millions worldwide in recent years. However, the epidemic's impact on the residents of the southern Libyan region has not been assessed. To investigate the spread of COVID-19 among the population, a study was conducted from March to June 2021. The study involved 146 people, 97 of whom were infected with COVID-19 and 49 were not infected. A complete blood count (CBC) and multivariate statistical analysis were used to determine the extent of the epidemic's spread in the study area. The CBC analysis used China's Tecom Science Corporation, model number TEK-5000. The results revealed that males (58.76%) were more affected than females (41.24%). The most affected age group was those under 46 (53.6%). The T-test analysis showed significant differences (p > 0.01) for each Red blood cell count (RBC), Mean corpuscular haemoglobin (MCH), Mean corpuscular haemoglobin concentration (MCHC), Red cell distribution width (RDW), Platelet count (PLT), White blood cell count (WBC), Platelet count (PLT), and granulocytes (GRA). However, the Hematocrit (HCT) was less than the significance level (P < 0.05), and there was no significant difference (P > 0.05) for Hemoglobin (HGB), Mean corpuscular volume (MCV), Lymphocyte (LYM), and Monocyte (MON) compared to the uninfected group. This study indicates that COVID-19 infection significantly affects the average values of blood tests, and changes in these values may cause complications for patients. Therefore, monitoring these changes in blood values is crucial to reducing the death rate among the infected.

**Keywords:** Complete Blood Count; COVID-19; Multivariate statistical analysis; infected; uninfected; T-test.

# **Introduction**

The COVID-19 pandemic, discovered in Wuhan, China 2019, has caused widespread concern. Millions of people have been infected with the disease, quickly spreading globally [1,2]. COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), primarily affects the respiratory system [3]. The disease has severely impacted life's health, social, and economic aspects [4,5]. While most individuals recover within a few days after experiencing mild symptoms such as fever, dry cough, and altered sense of taste and smell [6,7], patients with acute symptoms, especially

those with pre-existing chronic conditions, can develop pneumonia and acute respiratory distress syndrome within days of contracting COVID-19, leading to increased mortality rates [7,8]. Although initial reports only linked COVID-19 to pneumonia, accumulating data reveals that coagulopathy and intravascular coagulation are also common among those infected and contribute to the high mortality rate [9,10]. Certain groups, including smokers, alcoholics, and those with a history of similar illnesses, are more susceptible to the disease. Elderly individuals with chronic conditions are more vulnerable to COVID-19 than younger,

healthier people [8,11]. Moreover, COVID-19 patients who are older and have diabetes, cardiovascular disease, or obesity are at a higher risk of hospitalization and death compared to those without these conditions [12,13]. Furthermore, older COVID-19 patients with diabetes, cardiovascular disease, or obesity are at a higher risk of hospitalization and death compared to those without these conditions [12,13]. Laboratory tests, such as a Complete Blood Count (CBC), provide crucial information about the stage and severity of COVID-19. Studies show that COVID-19 patients typically experience changes in red blood cells, haemoglobin levels, hematocrit levels, mean corpuscular volume, and monocyte and eosinophil levels. The average platelet volume is also a prognostic factor for COVID-19 patients [14]. Additionally, the concurrent consumption of alcohol and smoking is linked to more severe cases of COVID-19. Studies by Akman et al. [15] and Shivakumar et al. [16] assess the effectiveness of biomarkers from peripheral blood samples in diagnosing COVID-19 for patients visiting the emergency department. They find no significant difference between the positive and negative test groups regarding lymphocyte and platelet values (p>0.05). However, another study by Shivakumar et al. [16] identifies significant differences between infected and uninfected individuals in the neutrophil-to-lymphocyte ratio (NLR), platelet count, haemoglobin levels, and leukocyte count ( $p<0.05$ ). The NLR is approximately 1.8 times higher in COVID-19 patients who survive than usual, differing from the trends observed in uninfected individuals. These findings are further supported by [17], who report that critically ill COVID-19 patients exhibit considerably higher NLRs than the uninfected group. In 2021, Pozdnyakova et al. [18] conducted a study investigating the clinical significance of changes in numerical peripheral blood parameters in predicting outcomes for COVID-19 patients; they also compared these changes between critical cases of COVID-19-positive and COVID-19 negative patients, and the study revealed significant variations in the white blood cell counts among all COVID-19 patients, which differed depending on the severity of their cases.

The first case of COVID-19 in Libya was reported on March 24, 2020. Initially confined to the southern region, the outbreak eventually spread to the western and eastern parts of the country. Estimates suggest COVID-19 has affected between 390,000 to 1.3 million people in Libya, accounting for approximately 14 to 20% of the population [19]. The Coronavirus (COVID-19) has spread frighteningly among people, forcing many residents to undergo a test to ensure they are not infected. It was necessary to find a fast and reliable way to verify this. Therefore, this study aimed to use the complete blood analysis (CBC) method to determine the possibility of infection with this virus.

## **Materials and methods**

### *Study area*

The study was conducted from March to June 2021 in the Al-Shatti region of southwest Libya, approximately 700 km south of Tripoli and 60 km north of Sebha. The Al-Shatii district is situated between latitudes 23° to 28.5° N and longitudes 10° to 16° E, with a population of roughly 100,000 individuals [20]. Blood samples for complete blood count (CBC) analysis were collected from patients admitted to the isolation centres in Brack and Algorda.

#### *Collection of blood samples*

This study included 146 patients, with 97 testing positive for COVID-19 via PCR and 49 testing negatives at the Brack Isolation Centre (BIC) and the filtration centres in Brack, Al-Qardah, and Al-Disa. The sampling technique is based on the procedure commonly used by other researchers; medical staff members took blood samples from patients admitted to the isolation centres who agreed to be part of this study, while the reference blood samples were taken from people who had no symptoms of convicted-19. Blood samples were collected using test tubes containing EDTA anticoagulant and were subsequently analyzed on the same day using a TEK-5000 CBC analyzer from Tecom Science Corporation, China.

#### *Statistical Analysis*

A multivariate analysis was conducted to examine the relationships between various CBC analyses. The Pearson correlation coefficient was used to measure the variability between the parameters and identify any correlations between them [21]. The data was analyzed using multivariate statistical analysis, which included descriptive statistics, correlation coefficients, and principal component analysis (PCA). Additionally, factor analysis, hierarchical cluster analysis (HCA), and T-test analysis were performed to compare the haematological parameters of infected and uninfected individuals. The analysis was carried out using SPSS version 26.

## **Results**

#### **Descriptive analysis**

This study included 146 individuals and thoroughly examined the connection between infection and blood parameters. Out of these, 97 were infected (41.24% female, 58.76% male) with an average age of 47 years, and 49 were uninfected (61.22% female, 38.78% male) with an average age of 34 years. The complete blood count (CBC) analysis presented



in Table 1 indicated notable differences between infected and uninfected individuals. Specifically, the levels of red blood cells (RBC), hematocrit (HCT), platelets (PLT), white blood cells (WBC), monocytes (MON), and granulocytes (GRA) were found to be higher in infected individuals compared to uninfected ones. Conversely, uninfected individuals exhibited higher levels of haemoglobin (HGB), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), red cell distribution width (RDW), and lymphocytes (LYM) than their infected counterparts.

Furthermore, the platelet count (PLT) displayed a high standard deviation, particularly within the infected group. It is noteworthy that the coefficient of variation (CV%) for variables such as haemoglobin (HGB), red blood cells (RBC), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), and red cell distribution width (RDW) indicates a symmetrical distribution of these variables.

The degree of variation in CV values can be classified as follows: low  $(10\%)$ , moderate  $(10\%$  to 20%), high  $(20\%$  to 30%), and very high (>30%). Typically, CV values range from 5% to 50%, with values below 1% rare. Variables with a CV% lower than 20% indicate a symmetrical distribution [22]. When the CV% values are low, the mean values align with the median, indicating homogeneity in the collected specimens [23].

## **Multivariate statistical analysis**

#### *Correlation analysis*

Table 2 presents the results of the Pearson correlation coefficient analysis conducted on CBC and the age of infected individuals. The study reveals a strong positive correlation between HGB, RBC, HCT, MCV, MCH, and MCHC (r=0.701, 0.919, 0.494, 0.595, and 0.408), respectively. Additionally, there is also a strong positive correlation between RBC and HCT (r=0.773), HCT and MCV and MCH (r=0.527 and 0.493), MCV and MCH ( $r=0.786$ ), MCH and MCHC ( $r=0.538$ ), PLT and WBC, MON, GRA (r=0.403, 0.492, and 0.302, respectively), WBC, MON, and GRA (r=0.383 and 0.919, respectively), and MON and GRA (r=0.269).





Principle component analysis for infected people.



The analysis also shows a high negative correlation between HBC and RDW (r=-0.289), HCT and RDW and PLT  $(r=0.303$  and  $-0.222$ , respectively), MCV and RDW  $(r=0.348)$ , MCH and RDW  $(r=-0.294)$ , and a positive correlation between RDW and PLT (r=0.223), GRA and Age (r=0.205). Furthermore, there is a negative correlation between RBC and GRA (r=- 0.209), HCT and PLT ( $r=0.222$ ), MCH and RDW ( $r=0.294$ ), and MCHC and RDW (r=-0.229). In uninfected individuals, a strong positive correlation exists between HGB and RBC, HCT, MCV, MCH, and MCHC with correlation coefficients of 0.596, 0.861, 0.406, 0.571, and 0.391, respectively. Similarly, there is a positive correlation between RBC and HCT, PLT with correlation coefficients of 0.807 and 0.368, respectively. Additionally, MCV is positively correlated with MCH (r=0.760), MCH is positively correlated with MCHC ( $r=0.652$ ), and MCHC is positively correlated with RDW  $(r=0.419)$ . There is also a positive correlation between PLT and MON (r=0.573), and WBC is positively correlated with LYM, MON, and GRA with correlation coefficients of 0.705, 0.630, and 0.881, respectively.



Extraction Method: Principal Component Analysis.

Rotation Method: Varimax with Kaiser Normalization.

Rotation converged in 6 iterations.

Table 5 Principle component analysis for uninfected people.



MON (r=0.464), and MON is positively correlated with GRA (r=0.462). On the other hand, there is a high negative correlation between RBC and RDW ( $r=-0.419$ ), HCT and RDW ( $r=-0.440$ ), MCV and WBC, and MON with correlation coefficients of -0.376 and -0.430, respectively. Additionally, MCH is negatively correlated with PLT, WBC, MON, and GRA with correlation coefficients of -0.455, -0.392, -0.572, and -0.397, respectively. MCHC is negatively correlated with PLT and MON with correlation coefficients of -0.493 and -0.498, respectively. Moreover, RDW negatively correlates with PLT and MON, with correlation coefficients of -0.466 and -0.396, respectively. In addition, there is a positive correlation between RBC, LYM and MON, with correlation coefficients of 0.356 and 0.362, respectively. Furthermore, MCH is positively correlated with RDW (r=0.362), and LYM is positively correlated with GRA (r=0.308). Conversely, there is a negative correlation between RBC and MCV ( $r=0.313$ ) and MCV and GRA ( $r=0.302$ ).

Furthermore, 13 LYM is positively correlated with

#### *Principle Component Analysis (PCA)*

The dataset was analyzed using principal component analysis to uncover any hidden patterns. The study revealed four eigenvalues greater than 1.00 before and after rotation. By reducing the initial dimension of the COVID-19-infected individual dataset, four components - PC1, PC2, PC3, and PC4 were obtained, which account for 74.218% of the data variation. Table 3 displays the initial component matrix, with PC1, PC2, PC3, and PC4 explaining 30.388%, 20.362%, 14.592%, and 8.876% of the total variance, respectively. The dataset structure was examined by analyzing the loadings of components and rotated components in Table 4. The loading plots of the rotated components and data groups offered a more transparent and more readily understandable view of the results. PC1 exhibited the maximum MCH, MCV, MCH, and RDW loading in negative values, while PC2 showed loading by RBC, HCT, and HGB. PC3 had loading by GRA and WBC, and PC4 with PLT, MON, and LYM.

The initial dimension of the uninfected dataset was also reduced, with four components explaining 84.381% (Table 5). PC1 explained 35.919% and was loaded with MCHC, PLT, RDW, and MON. PC2 explained 24.308% and had loaded with HCT, HGB, and RBC.

PC3 explained 15.472% and was loaded with WBC, GRA, and LYM, while PC4 explained 8.682% and was loaded with MCV and MCH. The results highlight the differences between the PCA of CBC and the age of infected and uninfected people, which we attribute to the COVID-19 pandemic.

#### *Cluster analysis*

The clustering method involves identifying segments within a dataset and assigning each observation to a specific cluster. The aim is to minimize variation within a dendrogram (24). Two dendrogram clusters were identified, representing infected and uninfected individuals. For infected individuals (Figure 1), cluster A was further divided into two sub-clusters: sub-cluster A1 included HGB-HCT and RBC, while sub-cluster A2 consisted of MCV, MCH, and MCHC. Likewise, cluster B was subdivided into three smaller clusters: B1(i) contained WBC and GRA, B1(ii) included RDW, and B1(iii) comprised PLT-MON. The variables within each cluster were found to be comparable and correlated. Sub-cluster B2 contained the LYM variable. For uninfected individuals, the hierarchical clustering revealed two main clusters (Figure 2), A and B. Cluster A was divided into two sub-clusters: A1 included WBC-GRA, LYM, and PLT-MON, while A2 contained HGB-HCT and RBC. Cluster B was split into two sub-clusters: MCV-MCH and MCHC, while the other contained only RDW.

## *Independent samples T-test*

In Table 7, the results of a T-test show that individuals infected with COVID-19 have similar levels of HGB, MCV, LYM, and MON as uninfected individuals. The probability value is higher than the significance level of 0.05, indicating no significant differences in these parameters. However, levels of HCT, RBC, MCHC, MCH, RDW, PLT, WBC, and GRA differ significantly, with probability values lower than the significance level of 0.05.



Extraction Method: Principal Component Analysis.

Rotation Method: Varimax with Kaiser Normalization.

Rotation converged in 6 iterations.



**Figure 1** – Cluster analysis of individuals with COVID-19



**Figure 2** – Cluster analysis of uninfected individuals with COVID-19

## **Discussion**

This study found that the majority of COVID-19 cases were among males (58.76%) with an average age of 47. In contrast, another study reported an equal ratio of male-to-female infection [25], possibly because males are more susceptible to COVID-19 infection than females, possibly because of biological differences in the immune system and genetic factors [26, 27]. Additionally, lifestyle factors such as smoking, drinking alcohol, and not following recommended social distancing regulations contribute to the higher infection rate in males [28]. On the other hand, females have been reported to behave more responsibly towards the COVID-19 crisis than men [26], which is consistent with other studies [28-30].

The study also found differences between infected and uninfected individuals through cluster analysis. Grouping of HGB-HCT in one cluster was acceptable since HGB and RBC are used to calculate HCT [31, 32], which could be attributed to the significant impact of COVID-19 on HGB, HCT, and RBC [33]. COVID-19 can lead to respiratory distress, affecting the blood's oxygen-carrying capacity and leading to hypoxia [34]. It may also directly infect bone marrow elements, resulting in abnormal hematopoiesis or triggering an autoimmune response against blood cells [35]. The second variable affected by COVID-19 was WBCs, which could be attributed to various factors, including an induced inflammatory response, immune system activation, and direct infection of immune cells, leading

to changes in WBC levels, including MON and LYM, causing their dysfunction [36]. T-test analysis showed higher RBC and HCT levels in infected patients compared to MCH and MCHC levels in uninfected patients. Previous studies [29, 37] have reported significantly lower RBC levels in severely ill patients. Similarly, Berzuini et al. [38] have reported a decline in RBC among COVID-19 patients, while Mei et al. (2020) [39] found considerably lower RBC, HGB, and HCT levels in severe cases. The results of our study show that the average HGB level is within the normal range, which differs from other studies. It has been suggested that COVID-19 patients have higher levels of HGB than uninfected individuals, possibly due to factors such as smoking and chronic diseases that were not excluded from the study by Usul et al. [17]. The average MCV values did not significantly differ between the two groups. Still, there was a notable decrease in the average RDW value among COVID-19 patients compared to uninfected individuals, contradicting previous studies [29, 40]. Additionally, it was reported that the morphological parameters of RDW were significantly higher in patients with severe COVID-19 [41]. The results also indicated a significant increase in the overall white blood cell (WBC) count in COVID-19 patients. On the other hand, other studies suggest that specific changes in blood cells can help diagnose and predict the progression of COVID-19 in patients infected with SARS-CoV-2 [29, 42]. COVID-19-positive patients have higher rates of anaemia and thrombocytopenia compared to those who test negative [43]. The results showed no significant difference in lymphocyte (LYM) levels between the two groups. Still, lymphopenia is commonly observed in COVID-19 patients [18, 44, 45] and is often associated with the severity of COVID-19 infection [46], which is consistent with findings reported by [29]. The results also demonstrated a significant increase in platelet (PLT) levels for the infected group, contrasting with previous reports. The monocyte (MON) count did not show a significant difference between the two groups, contradicting previous reports which indicated a substantial reduction in monocyte counts in COVID-19 patients [47]. Monocytes typically migrate to infection sites to combat pathogens, which can further decrease their blood levels [48]. In severe cases of COVID-19, the number of monocytes in the bloodstream may decline even more. Patients with severe symptoms have been found to have lower monocyte levels compared to those with milder symptoms, suggesting a potential role for monocytes in the progression of the disease [45, 48]. The immune system's response to the virus can lead to immune fatigue and monocyte exhaustion [49].

Moreover, COVID-19 can trigger a cytokine storm, an excessive immune response that damages healthy tissues, leading to monocyte death and reduced blood levels [49]. Increased granulocyte (GRA) in COVID-19 patients indicates severe respiratory tract infections and potential central nervous system

involvement. Conversely, recovered patients may exhibit lower GRA levels, possibly due to decreased immunological activity [35]. Furthermore, COVID-19 infection can cause variations in GRA, leading to changes in blood test results [50].

# **Conclusion**

The study used various statistical analysis techniques such as correlation coefficient, principal component analysis, cluster analysis, and T-test to distinguish between the Complete Blood Count (CBC) profiles of COVID-19-infected and uninfected individuals. The findings suggest that CBC analysis is valuable for diagnosing infection and assessing disease severity. Regular CBC monitoring is essential for observing changes in COVID-19 patients, potentially reducing the mortality rate. A CBC test can quickly determine disease severity when RT-PCR testing or trained medical personnel are unavailable. The results indicate that COVID-19 significantly impacts the health of those infected, with older individuals being the most affected and men showing greater susceptibility to the disease than women. Complications such as increased red blood cell count and hematocrit concentration can present patient problems, while elevated platelet numbers may lead to blood clots. Consequently, the study supports CBC analysis as a reliable method for predicting COVID-19 infection and determining its severity.

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