Research Article

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Haematological Manifestations of COVID-19 in Hypertensive Patients: A Retrospective Cohort Study

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ABSTRACT

Background: Alteration in haematological parameters is identified as critical early indicators of COVID-19. Hypertension (HTN) has been linked to an increased severity of COVID-19. The goal of this study is to investigate the numerous haematological factors in COVID-19 positive hypertensive patients in order to intervene early and improve patient outcomes.

Methods: In this retrospective cohort analysis, the medical e-records of 54 COVID-19 patients with HTN were evaluated. These patients' demographic and analytical data were analysed.

Results: Of the 54 hypertensive patients, 37.04 percent were asymptomatic at the time of presentation. Anaemia was observed in 20.37 percent of the patients across the haematological parameters. 63 percent had a high red-blood-cell count, and 25.93 percent had a high red-blood-cell-distribution-width (RDW). There was 14.81 percent thrombocytosis and 7.41 percent thrombocytopenia. 44.44 percent had a large platelet distribution width (PDW) and 57.41 percent had a large mean platelet volume (MPV). Neutropenia affected 14.81 percent of the population, whereas lymphocytopenia affected 16.67 percent.

Conclusion: Hypertensive COVID-19 positive individuals have been shown to have substantial hemopoietic-system signs with varying haematological profiles. Recognizing the significance of these variables early in primary care can assist physicians in making clinical decision and directing early referral to secondary-care facilities, which can help improve prognosis.

KEYWORDS: Hypertension; Preventative Medicine; Public Health; Risk factor; SARS-CoV-2

ABBREVATIONS: COVID-19: Corona Virus Disease 2019; WHO: World Health Organization; RAK-HC: RawdatAl Khail Health Site; ECG: Electrocardiogram; PHCC: Primary Health Care Corporation; CBC: Complete Blood Count; CMP: Comprehensive Metabolic Panel; CRP: C-reactive Protein Test; RDW: Red-Blood-Cell-Distribution-Width; PDW: Platelet Distribution Width; MPV: Mean Platelet Volume; ACE2: Angiotensin-Converting Enzyme

INTRODUCTION

The Coronavirus disease 2019 (COVID-19) infected approximately 530 million individuals globally and claimed the lives of over 6.3 million people between the commencement of the pandemic as of Mai 28th, 2022 [1]. Because of the rapid spread of COVID-19, the World Health Organization (WHO) has suggested that public health precautions be implemented, such as isolating anyone suspected of having the disease for 14 days. To combat the spread of COVID-19 [2-6], many countries have implemented "social distancing" and "lock-downs" of entire populations, with differing degrees of severity. These approaches hinder persons' movement, daily activities [7,8], and social connections [9]. Quarantined individuals had a higher prevalence of psychological discomfort and disorder symptoms (e.g., sadness, anxiety, negative feelings,

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emotional weariness, somatic symptoms, panic disorder); [7,8]. Physical exercise, which has been found to benefit overall health [10-12], may be more difficult to do during confinement [12-15].

Previous research has linked the occurrence of comorbidities in COVID-19 patients to poor clinical outcomes [16]. According to recent research, around 20-51 percent of COVID-19 patients have at least one comorbidity [17-19] with hypertension (16.9 percent) and diabetes mellitus (8.2 percent) being the most common [20]. A pooled analysis found that hypertension is associated with a greater risk of severe or fatal COVID-19, particularly in the elderly [21]. It is widely accepted that patients with comorbidities are more likely to become infected with SARS-CoV-2 and acquire severe disease. The most prevalent comorbidity among COVID-19 patients is hypertension, which is associated with an increased risk of infection as well as poorer outcomes and prognosis [22-27]. The fact that hypertension is the most common comorbidity in COVID-19 patients is not surprising given that the illness is more common and severe in the elderly, and hypertension is common in the elderly, hence hypertension can be seen in many COVID-19 cases. However, it is unknown if uncontrolled blood pressure is a risk factor for contracting COVID-19 and developing severe disease [27].

A meta-analysis found that patients with underlying cardiovascular disease, such as hypertension, are more susceptible to MERS-CoV infection [28], and some studies have found that patients with cardiovascular disease, particularly hypertension, are more likely to become infected with COVID-19 and develop more severe disease, but more research is needed in this area [29]. Although hypertension is the most prevalent comorbidity among COVID-19 patients, and some studies have linked it to poorer outcomes [22-25,27], there is little data on prognostic variables among COVID-19 patients with underlying hypertension to predict probable outcomes. So, in this study, we aimed to compare the epidemiologic, clinical, and laboratory differences between COVID-19 patients with and without underlying hypertension, and we identified some prognostic factors to predict disease severity and other possible outcomes in patients with pre-existing hypertension.

We are seeing more data linking hematological abnormalities and comorbidities to the severity of COVID-19 and the length of hospitalization. Nonetheless, in different countries, elaborative investigations on the connection of hematological abnormalities with the severity and length of hospitalization of COVID-19 patients are rare. Furthermore, the severity and mortality of coronavirus infection vary by country due to the virus's local mutation in different geographical areas [23]. As a result, most studies have limits based on geographical consideration, parameters evaluated, and the predictive significance of altered variables. For example, Bangladesh is a highly populated country with a sizable elderly population [24,25] where 7.7% of the entire population is over the age of 60, and 53.8 percent of older persons have comorbidities such as blood diseases, hypertension, diabetes, COPD, and so on [26-31]. Indeed, an insufficient number of health care service professionals and limited healthcare facilities exacerbate the situation [31]. As a result, the study's goal was to evaluate the hematological parameters of hypertension patients sent to Rawdat al khail Health Center in Qatar during the month of July 2020.

METHODS

This is a retrospective data analysis cohort research that included patients who were diagnosed with COVID-19 as well as hypertension according to their medical e-records. The patients in this investigation were referred to RawdatAl Khail Health Site (RAK-HC), a Ministry of Public Health-designated COVID-19 testing center in Doha, Qatar (MOPH). The research period was July 2020, and demographic and laboratory data for these patients were gathered from their medical e-records after the Primary Health Care Corporation (PHCC) research department anonymized and disclosed patient details. The PHCC ethics committee authorized the study under the reference number PHCC/DCR/2020/08/091. Of the 1054 COVID-19 positive patients seen at RAK-HC in July 2020, 54 were hypertensive and had additional investigations, including a blood test, electrocardiogram (ECG), and a chest X-ray, as well as a thorough clinical assessment, to further assess the severity of COVID-19 infection, dictating further management of this group of patients. This patient group's blood tests included a complete blood count (CBC), a comprehensive metabolic panel (CMP), liver function tests (LFT), urea and electrolytes, random glucose, and a c-reactive protein test (CRP). In this study, we solely looked at the hematological parameters of this group.

RESULTS

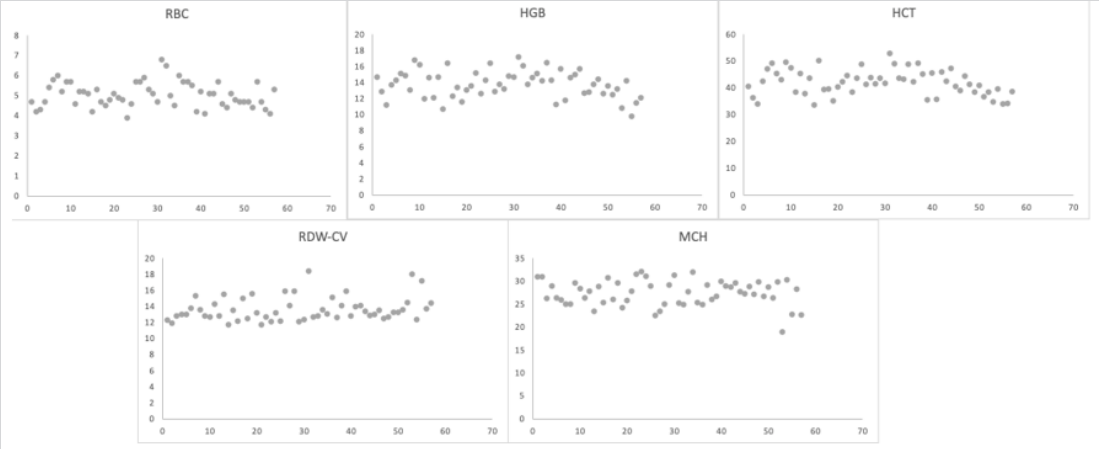

Figure 1: Red Blood Cells (RBC), Haemoglobin (HB), Haematocrit (HCT), Red blood cell distribution width (RDW), and mean corpuscular Haemoglobin (MCH) distributions among hypertensive COVID-19 Patients.

Amongst the investigated patients, seventy had a co-diagnosis of HTN, thus being included in this study (N = 54; Age: 54.95±8.84; Sex: 62.96% males and 37.04% females). In the present study, we investigated patients with HTN who COVID-19 were positive at RAK-HC and analyzed their hematological parameters. Patients with missing or incomplete lab results and those who were younger than 18 years old were not included in this study. This study was particularly aimed at investigating their hematological parameters at presentation in primary care. Of the 54 hypertension patients, 37.04 percent were asymptomatic at the time of presentation. Anemia was observed in 20.37 percent of the patients across the haematological parameters (Figure 1; Table 1). 63 percent had a high red-blood-cell count, and 25.93 percent had a high red-blood-cell-distribution-width (RDW); (Figure 1; Table 1). There was 14.81 percent thrombocytosis and 7.41 percent thrombocytopenia (Figure 2; Table 1). 44.44 percent had a large Platelet Distribution Width (PDW) and 57.41 percent had a large Mean Platelet Volume (MPV); (Figure 2; Table 1). Neutropenia affected 14.81 percent of the population, whereas lymphocytopenia affected 16.67 percent (Figure 3; Table 1).

Table 1: Haematological disorders in hypertensive COVID-19 patients.

Haematological Parameters	Abnormal High (n)	Abnormal Low (n)	Abnormal High (%)	Abnormal Low (%)	Normal Range
RBC (106/mm^3)	34	0	62.96	0	(3.8 - 4.8)
Hgb (g/dl)	11	11	20.37	20.37	(12.0 - 15.0)
Hct (%)	13	7	24.07	12.96	(36.0 - 46.0)
MCV (fL/cell)	0	19	0	35.19	(83.0 - 101.0)
MCH (pg/cell)	1	23	1.85	42.59	(27.0 - 32.0)
MCHC (gm/dL)	4	15	7.41	27.78	(31.5 - 34.5)
RDW-CV (%)	14	0	25.93	0	(11.6 - 14.5)
PL (/mcL)	8	4	14.81	7.41	(150 - 400)
MPV (fL/cell)	31	0	57.41	0	(7.4 - 10.4)
PDW (fL/cell)	24	4	44.44	7.41	(9.4 - 10.6)
WBC (109/L)	5	4	9.26	7.41	(4.0 - 10.0)
NE (109/L)	5	8	9.26	14.81	(2.00 - 7.00)
LY (109/L)	3	9	5.56	16.67	(1.00 - 3.00)
MO (109/L)	2	7	3.7	12.96	(0.20 - 1.00)
EOS (109/L)	0	0	0	0	(0.0 - 0.5)
BAS (109/L)	0	10	0	18.52	(0.02 - 0.10)

BAS: Basophiles; EOS: Eosinophils; HB: Hemoglobin; HCT: Haematocrit; LY: Lymphocytes; MCH: Mean Corpuscular Haemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; MCV: Mean Corpuscular Volume; MO: Monocytes; MPV: Mean Platelet Volume; NE: Neutrophils; PDW: Platelet Distribution Width; PL: Platelet Count; RBC: Red Blood Cells; RDW: Red Blood Cell Distribution Width; WBC: White Blood Cell Count

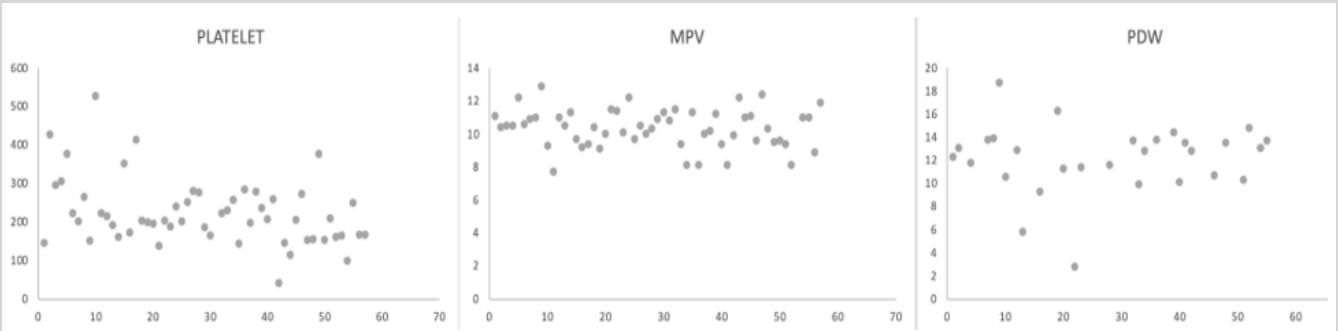

Figure 2: Platelet count (PL), Mean platelet volume (MPV) and Platelet distribution width (PDW) distributions among hypertensive COVID-19 Patients.

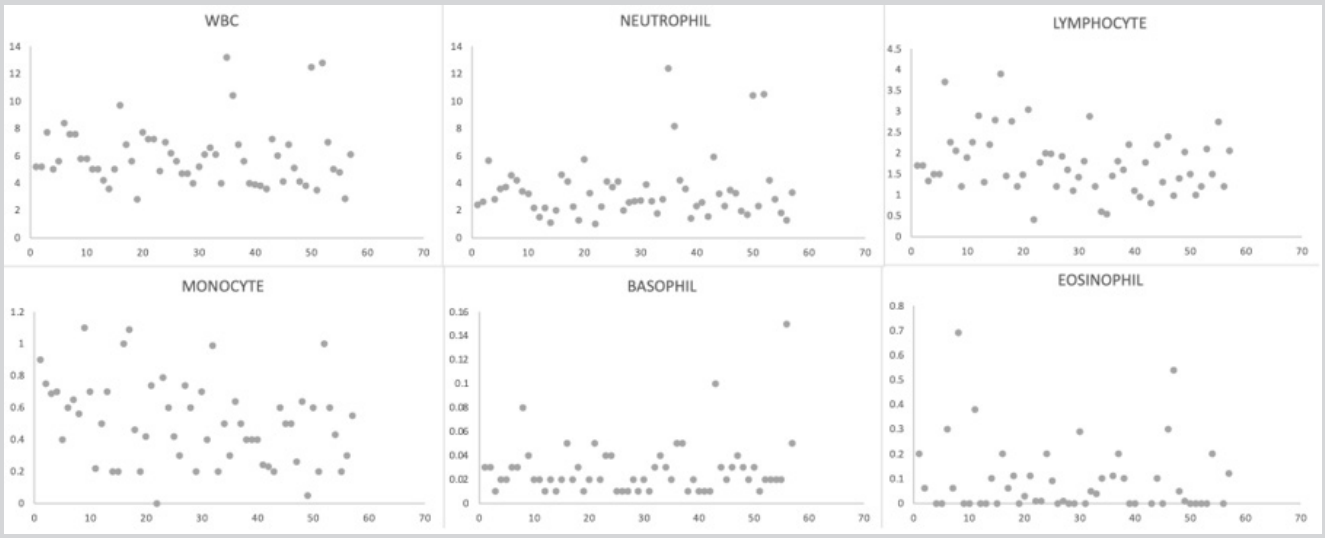

Figure 3: White blood cells (WBC) and subpopulations distributions among hypertensive COVID-19 Patients.

DISCUSSION

COVID-19 patients developed a variety of hematological alterations, including leukocytosis, decreased lymphocyte count, raised D-dimer levels, neutrophilia, thrombocytopenia, eosinopenia, and basopenia [31]. Furthermore, patients with severe disease exhibited more obvious test abnormalities than those with non-severe disease. In our study, which looked at those parameters, many anomalies were found in the hematological parameters of COVID-19 hypertensive patients. According to our data, anemia was found in 20.37 percent of the patients across all hematological parameters.63% had a high RBC count, and 25.93% had a high RBC distribution width (RDW). Thrombocytosis was found in 14.81 percent, and thrombocytopenia was found in 7.41 percent of the investigated population. 44% had a wide platelet distribution width (PDW), and 57.41% had a high mean platelet volume (MPV). Among the population, neutropenia impacted 14.81 percent of the population, while lymphocytopenia affected 16.67 percent of the population. Certainly, with the increasing prevalence of COVID-19 transmission [32], it is critical to produce thorough data on COVID-19 severity in order to assess the mortality risks. COVID-19 severity can be determined using hematological markers and coexisting disease [33]. As a result, by conveniently monitoring such prospective indications, we can determine the severity and mortality risks of patients. In our findings, we looked at certain hematological parameters in COVID-19 patients of different ages with high blood pressure.

Several case series and retrospective cohort studies have shown hypertension as a possible risk factor for the occurrence and severity of the novel coronavirus (SARS-CoV-2)-associated disease (COVID-19). The topic is relevant because, according to the Global Burden of Disease survey, about one billion individuals worldwide are predicted to have hypertension. Given the high infectivity rates of SARS-CoV-2, a probable connection between COVID-19 and hypertension is concerning. Furthermore, antihypertensive medications, particularly renin-angiotensin-aldosterone system (RAAS) inhibitors, may impact the natural course of COVID-19 infection. Not only do these relationships hold epidemiologically, but a mechanistic scenario may also exist. Hypertension and antihypertensive medicines can boost the expression of transmembrane angiotensin-converting enzyme (ACE)-2 receptors, the viruses' entrance targets, allowing them to infect more people. On the other hand, a rise in ACE-2 may be protective because the ACE-2-angiotensin 1-7/Mas pathway can reduce inflammation and stop blood clots [34,35].

Different abnormalities in the levels of hematologic parameters have been linked to a greater chance of COVID-19 severity [34,35]. Terpos et al. [36] examined hematological parameters in COVID patients and discovered certain irregularities in COVID-19 patients. Other research [37] showed that there is a link between high CRP and ferritin levels in COVID-19 patients, which backs up the current findings. After SARS-CoV-2 enters the bloodstream, it primarily affects the angiotensin-converting enzyme (ACE2), a SARS-CoV-2 receptor expressed in many organs such as the liver, heart, and gastrointestinal system. The CT scan result demonstrates changes in the worsening scenario after 7-14 days of illness. At this time, lymphocyte counts fall, and inflammatory cytokine levels rise, worsening patients' conditions [38]. Lymphopenia is prevalent in critically ill patients and correlates with COVID-19 severity [39]. Furthermore, along with increased leukocytes, COVID-19 patients usually have decreased basophils, monocytes, lymphocytes, eosinophils, and platelets [40]. According to research, neutropenia has been observed in COVID-19 patients who required ICU care. As a result, the neutrophil-to-lymphocyte ratio can be used to predict the severity of COVID-19 patients [41]. Several studies [39] found that thrombocytopenia due to low platelet count occurred in a considerable proportion of individuals who required hospitalization. Lippi et al. [42] looked at four different studies that showed that COVID patients' Hb levels are going down, which is a factor in the disease getting worse. A meta-analysis of 21 studies on 3,377 patients found a substantial correlation between COVID-19 and aberrant hematological markers [43]. As a result, hematological abnormalities are closely related to the severity of COVID-19, the length of hospitalization, and the need for ICU assistance.

Our findings also revealed that 25.93% had a high RDW. Indeed, RDW is a routine component of a complete blood count test. RDW measures the variance in individual red blood cell (RBC) volumes, which fluctuate from one cell to the next and within the same cell during its 115-day lifespan [44]. Elevated RDW is linked to an increased risk of all-cause mortality, mortality from heart disease, pulmonary disease, sepsis, influenza, and cancer, complications

from heart failure, the severity of coronary artery disease and viral hepatitis, advanced stage and grade for many cancers, and the development of diabetes, chronic obstructive pulmonary disease, stroke, anemia, and many other conditions [45,46]. RDW seems to be a universal sign of illness that can provide quantitative risk stratification for everyone. This could be especially helpful in the case of a new and unknown disease.

RDW is the RBC volume coefficient of variation, or the SD divided by the mean. As a result, an increase in RDW must be accompanied by a drop in mean RBC volume (MCV), an increase in RBC volume variance, or both. Previous research [47,48] has uncovered evidence that RDW elevation is driven by delayed clearance of older RBCs in some specific situations. Because RBCs typically lose cellular volume as they age, the persistence of these older, smaller cells increases volume variation, and this clearance delay coincides with and compensates for a net decline in RBC production [48]. These studies imply that an elevated RDW may reflect a clinical situation in which RBC synthesis and turnover have decreased in the context of enhanced production and turnover of leukocytes or platelets, as would occur in inflammation. Even though there is no clear reason why RDW goes up, there is evidence that RDW can be used to classify patients with the same acute disease according to their risk.

As a result, numerous studies have highlighted the potential benefit of employing RDW for a differential diagnosis of pneumonia [49,50] or as a marker of complication rates in SARS-CoV-2 infection [51,52], either directly or as a component of a machine learning framework. Recent small-scale studies have used RDW along with the neutrophil-lymphocyte ratio or hemoglobin in multivariate models for COVID-19 differential diagnosis.

The particular process or mechanisms causing the RDW change related to COVID-19 are unknown. Because RDW is a generic sign of general illness [46], it is unlikely to be causally related to COVID-19 disease development. As previously stated, COVID-19 is related to abnormal turnover in all WBC lineages, as well as altered platelet dynamics in COVID-associated coagulopathy. The connection between elevated RDW and COVID-19 severity may be consistent with prior results (in non-COVID-19 cohorts), implying that RDW can become elevated when RBC production kinetics have slowed in the context of increased WBC and platelet kinetics [46]. Patients with a variety of underlying acute and chronic illnesses would be expected to have a higher baseline RDW, and it is possible that the RDW measured at admission is a nonspecific summary marker of the presence of these illnesses, which have been linked to elevated RDW and may complicate the COVID-19 clinical course.

Potential Limitations of the Study

The present study has few drawbacks. The study included COVID-19 patients from Rawdat al Khail Health Center only and not from all the COVID-19 hypertensive population of Qatar. Also, the subsequent follow-up information was not available in this study. Additionally, the small number of patients investigated in the present study constitutes another main limitation.

CONCLUSION

Physicians continuously monitor several blood parameters to measure the severity and mortality risks of COVID-19 patients. Among the altered haematological parameters, elevated RBC, MPV, and PDW levels might be used as predictable markers to assess the COVID-19 severity. Also, these parameters might help to evaluate the treatment plan and decisions in the hospital setup. Therefore, we recommend these parameters as factors for early detection of COVID-19 severity that facilitates treatment decisions. This topic needs to be explored further for quick initiation of treatments for secondary care and optimization of COVID-19 treatment.

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DECLARATION OF INTEREST

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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AUTHOR CONTRIBUTIONS

Conception and design - Imen MBAREK, Lelna MANU, Shumoos saad ABED, Abdullah AL NAAMA.

Analysis and interpretation of the data – Imen MBAREK, Lelna MANU.

Drafting of the paper - Imen MBAREK, Lelna MANU, Shumoos saad ABED, Abdullah AL NAAMA.

Revising it critically for intellectual content- Shumoos saad ABED.

The final approval of the version to be published - Imen MBAREK, Lelna MANU, Shumoos saad ABED, Abdullah AL NAAMA.

All authors agree to be accountable for all aspects of the work.

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