Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Clinical and hematologic presentations of adults with COVID-19 patients in Jeddah: A case control study

Fatemah O. Kamel [a], Rania M. Magadmi [a,*], Sulafa T. Alqutub [b], Maha Badawi [c], Fatin Al-Sayes [c], Mazen Badawi [d], Tariq A. Madni [d], Areej Alhothali [e], Ehab A. Abozinadah [f], Soheir Adam [c,g]

[a] Pharmacology Department, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia
[b] Department of Family and Community Medicine, Faculty of Medicine, University of Jeddah, Jeddah, Saudi Arabia
[c] Hematology Department, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia
[d] Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia
[e] Department of Computer Science, Faculty of Computing and Information Technology, King Abdulaziz University, Jeddah, Saudi Arabia
[f] Department of Information Systems, Faculty of Computing and Information Technology, King Abdulaziz University, Jeddah, Saudi Arabia
[g] Department of Medicine, Faculty of Medicine, Duke University, Durham, North Carolina, United States

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2), is associated with significant morbidity and mortality. The clinical features of COVID-19 were mentioned in previous studies. However, risk factors for COVID-19 are not fully recognized. The aim of this study is to characterize risk factors and clinical features of COVID-19 disease in Jeddah, Saudi Arabia.

Methods: A retrospective, chart-review, case-control study was conducted at King Abdulaziz University, Jeddah, Saudi Arabia. Demographic, clinical, radiological, and laboratory data on patients diagnosed between March 18 and May 18, 2020 were collected and analyzed.

Results: We reviewed medical records on 297 suspected cases of COVID-19. Of these, 175 (59%) tested positive for COVID-19 by polymerase chain reaction (PCR) and considered as cases, while 122 (41%) tested negative and considered as control. COVID-19 positive cases were more likely to be males, and non-health care providers. Hypertension (15%), diabetes (10%) and two or more concurrent comorbidities (54.4%) were more prevalent among COVID-19 patients. Patients presented with fever, cough, and loss of taste/smell were more likely to test positive for COVID-19 ($P = 0.001, 0.008, 0.008$; respectively). Radiological evidence of pneumonia was associated with confirmed COVID-19 disease ($P = 0.001$). Shortness of breath and gastrointestinal symptoms were not associated with the risk of COVID-19 at presentation. On admission, white blood cells, neutrophils, lymphocytes, eosinophils, basophils, and platelets were significantly lower among COVID-19 patients compared with controls. Surprisingly, D-Dimer levels were lower among COVID-19 positive patients when compared with controls.

Conclusion: Male gender, hypertension, and diabetes are the most commonly observed risk factors associated with COVID-19 disease in Jeddah, Saudi Arabia. COVID-19 patient had significantly lower lymphocyte and neutrophil counts.

Introduction

Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) was initially recognized in December 2019 in Wuhan, China [1]. Within the ensuing weeks, SARS-CoV-2 spread across China and around the world, resulting in a global pandemic. The World Health Organization (WHO) declared that the outbreak was a Public Health Emergency of International Concern on the 30th of January 2020

* Corresponding author at: Pharmacology Department, Faculty of Medicine, King Abdulaziz University, P.O. Box 42751, Jeddah 21551, Saudi Arabia.
E-mail address: rmagadmi@kau.edu.sa (R.M. Magadmi).

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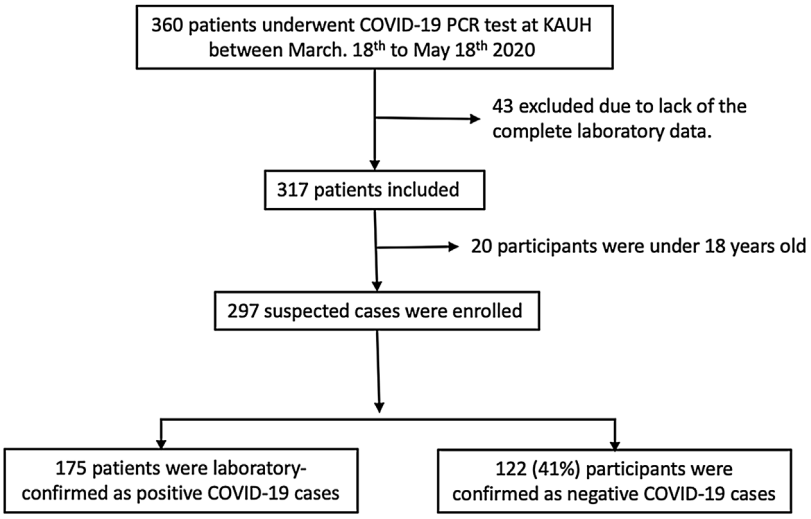

Fig. 1. Study flowchart.

[2]. On February 12, 2020, WHO officially renamed the SARS-CoV-2 infection Coronavirus Disease-19 (COVID-19) [3].

This highly contagious virus spread at an alarming rate around the world, and the first case of COVID-19 in Saudi Arabia (SA) was identified on March 2, 2020 [4]. Subsequently, many cases have been confirmed in different regions of SA. Various demographic and clinical factors have been associated with the risk of severe disease [5–7].

Rapid diagnosis and case isolation are crucial for slowing the spread and for outbreak containment [8]. Case recognition can rely on a series of clinical presentations that increase the likelihood of a positive diagnosis, including shortness of breath, cough, sore throat, and fever. However, these symptoms are also common in other respiratory infections, including bacterial pneumonia, influenza virus infections, or rhinovirus infections [9].

The gold standard method for the presence of COVID-19 is the real-time polymerase chain reaction (RT-PCR) for detecting the presence of the virus in nasopharyngeal swab. However, this test can be time consuming and delay the diagnosis. Subsequently, patient isolation may be delayed, which results in further spread of the infection.

Previous studies reported significant changes in various laboratory parameters, including lymphopenia, high C reactive protein levels, ferritin, and D-dimer among COVID-19 cases [7,9]. Another study has reported a significant leukopenia in around 30% of 24 asymptomatic COVID-19 cases [10]. However, most of the studies were conducted on a relatively small population.

Therefore, this retrospective case-control study identify the clinical and laboratory predictors of positive COVID-19 patients and risk factors for severity and outcomes. The results of this project will foster the prediction of disease and provide a great opportunity to explore novel diagnostic and prognostic factors to identify and treat the disease effectively.

Subjects and methods

Study design and data collection

This retrospective case-control study was conducted in King Abdulaziz University Hospital (KAUH), in Jeddah, SA. All the case and control participants were identified from hospital admissions. Demographic and clinical data of participants tested for SARS-CoV-2 by nasopharyngeal swab between March 18, 2020, to May 18, 2020 were extracted from the hospital's electronic medical information system. The recorded data included the participants' baseline demographic characteristics including: age, gender, nationality, and occupation. The clinical symptoms and signs on presentation, laboratory parameters, and underlying comorbidities, as well as the admission course and patients' outcome were obtained for analysis. Patients of <18 years and those with incomplete data were excluded. The protocol for this study was approved by the Institutional Ethics Committee and followed the ethical standards of the bioethics and research committee of the King Abdulaziz University. Ethics Reference No 271-20 on June 6, 2020.

The COVID-19 Score is a visual triage scoring system that has been released by the Saudi Ministry of Health (MoH) for the early prediction of patients with acute respiratory illness in the emergency departments [11]. The visual triage form consists of a nine-item scoring system divided into two parts. The first part is related to signs and symptoms at presentation, and the second part is related to the potential risk of exposure to COVID-19.

Laboratory procedures

COVID-19 diagnosis was confirmed by RT-PCR using nasopharyngeal swabs performed at the institute central lab. Laboratory investigations included: (1) complete blood count (CBC), differential white cell count, and blood group typing, (2) coagulation parameters, such as D-dimer, prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen, and 3) inflammatory markers, such as C-reactive protein (CRP), ferritin, and N-terminal pro b-type natriuretic peptide (NT-proBNP).

Sample size calculation

Open epi info (CDC, Atlanta) was used to calculate the required sample size for the case-control study. The calculated sample size was 360 participants who underwent COVID-19 PCR test (Fig. 1). A total of 63 participants were excluded. Forty-three of them were excluded because of missing laboratory data, and 20 participants were excluded for being under the age of 18. Among the 297 participants, 175 (59%) patients were confirmed positive for COVID-19 cases by RT-PCR testing (the case group) and 122 (41%) participants tested negative for COVID-19 (the control group). Patients from control group were symptomatic and admitted for other medical conditions. With the identified sample size of 297, the calculated power is 90.98%. 175 cases with 60% of exposure and 122 controls with 40% of exposure. The minimum detectable OR is 2.2.

Table 1
Demographic characteristics of COVID-19 PCR positive patients (cases group) and COVID-19 PCR negative (control group) (N = 297).

Characteristic		All patients N = 297 (%)	Positive COVID-19 PCR (cases group) N = 175 (%)	Negative COVID-19 PCR (control group) N = 122 (%)	Chi-Square Tests *P*-value
Age group	18–29	55 (18.5%)	31 (18.0%)	24 (20.0%)	0.291
	30–39	75 (25.3%)	3 7 (21.1%)	38 (31.1%)	
	40–49	58 (19.5%)	34 (19.4%)	24 (20.0%)	
	50–59	68 (23.0%)	49 (28.0%)	19 (15.6%)	
	60–69	27 (9.1%)	17 (10.0%)	10 (8.2%)	
	70–79	8 (2.7%)	4 (2.3%)	4 (3.3%)	
	80–89	4 (1.3%)	2 (1.1%)	2 (1.6%)	
	90–100	2 (0.7%)	1 (0.6%)	1 (0.8%)	
Gender	Male	180 (60.6%)	120 (68.6%)	60 (49.2%)	0.001*
	Female	117 (39.4%)	55 (31.4%)	62 (50.8%)	
Nationality	Saudi	78 (26.3%)	39 (22.3%)	39 (31.9%)	0.061
	Non - Saudi	219 (73.7%)	136 (77.7%)	83 (68.1%)	
Body Mass Index (N = 229)	<26	119 (52.2%)	77 (55.8%)	42 (46.2%)	0.331
	26–30	54 (23.6%)	31 (22.5%)	23 (25.3%)	
	>30	56 (24.5%)	30 (21.7%)	26 (28.6%)	
Job	Health care providers	39 (13.13%)	16 (9.1%)	23 (18.8%)	0.022*
	Non- health care providers	258 (86.9%)	159 (90.9%)	99 (81.1%)	

* $P < 0.05$ for chi-square were considered statistically significant, N = number of patients.

Statistical analysis

The socio-demographic results, clinical presentations, and comorbidities of patients are represented using descriptive statistics. Frequencies and percentages were reported for categorical variables. Continuous data were reported as mean ± standard deviation. Differences between groups were analyzed using Pearson's chi-square and odd ratio (OR) with 95% confidence interval (CI) to test categorical variables, and *t*-test for continuous outcome variables. Significance (*P-value*) was set at 0.05. Statistical analysis was performed with Social Sciences Statistical Package (SPSS) software version 21 (IBM, US).

Diagnosis prediction using machine learning algorithms

To assess the significance of the relevant demographical, clinical, and hematological parameters as predictors in diagnosing COVID-19 patients, two machine learning algorithms, namely logistic regression and naïve Bayes, were implemented. Both were trained on patients' characteristics to predict their COVID-19 test results (i.e., positive, negative). The machine learning approaches are implemented on 18 characteristics that show statistical relevance (*P*-value <0.07) in the *t*-test and chi-square test (Supplement 1). Both machine learning approaches were trained and tested using cross-validation techniques, and a grid-search algorithm was performed to choose the best hyper-parameters (regularization penalty: l1, solver: liblinear, and C:10) for the logistic regression model.

Results

Characteristics of study population

Demographic data for COVID-19 positive and negative groups are presented in Table 1. Most COVID-19 positive cases (28%) were between 50–59 years of age, while most COVID-19 negative participants (71.1%) were younger than 50 years old. However, there was no statistically significant difference in age ($P = 0.29$) between both groups.

COVID-19 positive cases were more likely to be males (68.6%) compared to (31.4%) COVID-19 female positive cases ($P = 0.001$). Conversely, COVID-19 positive cases were less likely to be health care providers (90.9%) compared with control group ($P = 0.02$).

Comorbidities in patients with and without COVID-19

Of 175 COVID-19 positive cases, 77 (44%) were known to have history of chronic diseases (Table 2). Almost half of this group (43 patients), had more than two comorbidities. The most common single comorbidity in COVID-19 positive cases was hypertension (15.6%), followed by diabetes (10.4%).

Clinical characteristics of study population

Table 3 shows the most common clinical presentations of COVID-19 cases and control groups. Patients who presented with a fever between 37.3–39 °C were significantly more likely to be COVID-19 positive than COVID-19 negative ($P = 0.001$). Likewise, patients who presented with cough or loss of taste/ smell were significantly more likely to be COVID-19 positive than negative (All $P = 0.008$).

As expected, evidence of pneumonia on chest x-ray showed a significant association with COVID-19 positive cases compared with control group ($P = 0.001$) (Table 3).

With regard to COVID-19 score, the most common reported score among COVID-19 positive cases in this study was 7 (31%), followed by 6 (27%). Patients with scores 7 or 6 were more likely to be COVID-19 positive ($P < 0.001$).

Hematological parameters in study population

Table 4 shows the comparison of hematological parameters for both the COVID-19 positive cases and control groups. On admission, COVID-19 positive cases showed a significantly higher in hemoglobin (Hb) levels compared with the COVID-19 negative cases ($P = 0.031$).

On the other hand, COVID-19 positive cases showed a significant decrease in mean white blood cells (WBC) count, as well as basophil, neutrophil, lymphocyte, and eosinophil counts compared with the controls (All $P < 0.05$). However, all parameters in COVID-19 positive group were within the normal range except the lymphocyte count. Similarly, there was a significant decrease in the platelet (PLT) count in COVID-19 positive patients compared to the control group ($P = 0.003$).

Surprisingly, COVID-19 positive patients showed a significantly lower level of D-dimer in contrast with control group ($P = 0.036$). Also, PT, international normalization ratio (INR), Fibrinogen, Ferritin, and CRP were lower among COVID-19 positive cases, but the

Table 2
The differences in co-morbidities among COVID-19 PCR positive patients (cases group) and COVID-19 PCR negative (control group) (N = 142).

Medical Hx	Positive COVID-19 PCR (cases group) N = 77 (%)	Negative COVID-19 PCR (control group) N = 65 (%)	*P* -Value
Respiratory diseases	2 (2.6%)	10 (15.4%)	0.001*
Malignancy	2 (2.6%)	6 (9.2 %)	
DM	8 (10.4%)	3 (4.6%)	
HTN	12 (15.6%)	3 (4.6%)	
Other chronic diseases	10 (13%)	18 (27.7%)	
>2 chronic diseases	43 (55.8%)	25 (38.5%)	

>2 chronic diseases may include one or more of the following: Hypertension (HTN), Diabetes Mellitus (DM), respiratory or malignant illness.
* *P*<0.05 for chi-square were considered statistically significant, N = number of patients.

Table 3
The differences in clinical presentations among COVID-19 PCR positive patients (cases group) and COVID-19 PCR negative (control group) N = 297.

Symptoms		Positive COVID-19 PCR (cases group) N = 175 (%) 1	Negative COVID-19 PCR (control group) N = 122 (%)	Chi-Square Tests *P*-value
Temperature	< 37.3 °C	107 (61%)	99 (81.1%)	0.001*
	37.3–39 °C	65 (37.1%)	22 (18%)	
	> 39 °C	3 (1.7%)	1 (0.8%)	
Cough (N = 180)		117 (66.9%)	63 (51.6%)	0.008*
Shortness of breath (N = 76)		46 (26.3%)	30 (24.6%)	0.742
Sore throat/ runny nose (N = 90)		52 (29.7%)	38 (31.1%)	0.791
Loss smell/taste (N = 14)		13 (7.4%)	1 (0.8%)	0.008*
GIT symptoms (N = 76)		51 (29.1%)	25 (20.5%)	0.093
Other symptoms (N = 7 0)		44 (25.1%)	26 (21.3%)	0.444
Chest X-ray positive for pneumonia (N = 154)		103 (67%)	12 (21%)	0.001*

* *P* < 0.05 for chi-square test considered statistically significant, N = number of patients, GIT = gastro-intestinal tract.

differences between cases and control were not statistically significant.

The ABO group and Rh status was only tested in 33 COVID-19 positive patients and 55 with controls. The most common blood group in COVID-19 positive patients was A (42.4%), followed by O (24.2%), B (18.2%), and AB (15.2%). The most common blood group among controls was O (43.6%), followed by B (29.1%), A (27.2%), and AB (1.8%). Most patients in both groups were Rh (D) positive: (97.9%) and (96.3%) in those with positive and negative COVID-19 PCR, respectively.

Mortality and clinical outcomes in study population

A total of 20 of the study population were admitted to the intensive care unit. Fourteen out of them were PCR positive patients. The mortality rates were around 7% and 2.5% in PRC positive and negative patients, respectively.

It is worth to mention that among 175 positive COVID-19 patients, only 2 patients had a thromboembolic event. Detailed demographic and clinical characteristics of those patients are listed in Supplement 2.

Machine learning-based diagnosis prediction

The machine learning models used in this study show an accuracy of 82% and 81% for diagnosing COVID-19 using Naïve Bayes and logistic regression, respectively. As shown in the naïve Bayes confusion matrix (Fig. 2a), the positive predictive value (PPV) is equal to 0.88 (21 out of 175 cases are misclassified as COVID 19 negative), and the negative predictive value (NPV) is equal to 0.75 (30 out of 122 cases are wrongly predicted as being COVID 19 positive). The sensitivity and specificity are equal to 0.84 and 0.81, respectively (note that in the two confusion matrices, 0 = negative COVID 19 PCR, and 1 = positive COVID 19 PCR). The heat map scale goes from black to beige color to indicate the number of instances starting from 20 to 160. In the logistic regression (LR) model, the PPV is equal to 0.83, NPV is equal to 0.78, sensitivity is equal to 0.84, and specificity is equal to 0.77 using a 0.5 threshold (Fig. 2b). This threshold can be adjusted to increase and decrease the PPV and NPV, as needed. The order of the most significant features in the LR model (Fig. 2c) shows the order of features' coefficients in the model estimated functions after normalization. These promising results can be further improved by increasing the dataset size and or using more advanced machine learning and pre-processing techniques.

Discussion

COVID-19 global pandemic represents a major worldwide health threat. It is associated with a myriad of morbidities and mortality. In this study, clinical and hematological characteristics of 175 COVID-19 positive cases from KAUH, Jeddah, SA were compared with controls to identify risk factors for COVID-19 infection.

Most COVID-19 positive cases in this study were 50–59 years old. This observation is in agreement with previous international studies that showed the average age of COVID-19 positive cases was 47–62 years [6,12]. Similarly, males were more likely to be COVID-19 positive, as in previous reports [6,12]. Such figures may be because of sex-based immune disparities or may be because of smoking habits and prevalence [13]. Another explanation of male gender prevalent in this study could be the fact that more females stayed at home during the law of curfew than males, which made males more exposed to the infection.

In global efforts against COVID-19, health care providers' shortages are significant. Awareness of the consequences of this shortage leads to other interventions considered extreme under normal circumstances [14]. About 41% of the 138 health-care providers reported acquired hospital infections in a single-center study in Wuhan [7]. Approximately half of the emergency room workforce tested positive in the Royal Gwent Hospital, Newport, Wales [15]. In contrast, only 13.13% of COVID-19 positive patients were health care providers in this study. However, Alsofayan et al. [5] reported

Table 4
Comparison of the hematological parameters between COVID-19 PCR positive patients (cases group) and COVID-19 PCR negative (control group) (N = 297).

Hematological Parameters		Normal range	Positive COVID-19 PCR (cases group) N = 175 (%)	Negative COVID-19 PCR (control group) N = 122 (%)	*t*-test *P*-value
CBC	Hb (g/dL)	12–15	13.24 (±2.162)	12.62 (±2.69)	0.031*
	RBC (M/uL)	4–5.4	4.94 (±0.81)	4.63 (±0.94)	0.433
	WBC (K/uL)	4.5–11.5	6.55 (±2.71)	9.28 (±5.94)	0.001*
	PLT (K/uL)	150–450	245.66 (±108.79)	284.63 (±106.46)	0.003*
	Basophils (K/uL)	0.01 0.08	0.02 (±0.02)	0.0496 (±0.06)	0.001*
	Neutrophils (K/uL)	2–7.5	4.09 (±2.44)	6.14 (±5.25)	0.001*
	Lymphocytes (K/uL)	1.5–4	1.08 (±0.73)	2.09 (±1.23)	0.002*
	Eosinophil (K/uL)	0.04–0.4	0.08 (±0.31)	0.25 (±0.31)	0.001*
	Monocytes (K/uL)	0.4–1	0.67 (±1.28)	1.39 (±7.13)	0.201
	Basophils (%)	0–2	0.39 (±0.32)	2.95 (±25.42)	0.284
	Lymphocytes (%)	20–45	28.84 (±13.29)	26.20 (±14.0)	0.108
	Eosinophil (%)	1–3	1.58 (±3.65)	3.60 (±10.90)	0.061*
	Monocytes (%)	2–11	9.08 (±3.96)	8.97 (±4.14)	0.819
Coagulation	D-Dimer (mg/l)	0–0.5	1.24 (±3.88)	3.04 (±4.27)	0.036*
	PT (Seconds)	9.4–12.5	12.54 (±3.08)	12.56 (±2.04)	0.961
	aPTT (Seconds)	25.1–36.5	31.38 (±5.19)	30.39 (±6.43)	0.256
	INR (Ratio)	0.85–1.3	1.14 (±0.31)	2.698 (±12.38)	0.315
	Fibrinogen (mg/dL)	200–393	456.78 (±178.29)	489.77 (±304.655)	0.778
Infection-related biomarkers	Ferritin (ng/mL)#	30–400	432.36 (±644.57)	553.93 (±1364.86)	0.29
	CRP (mg/L)	0–3	38.80 (±51.38)	40.74 (±44.55)	0.846
	NT-proBNP (pg/mL)#		1881.28 (±4908.82)	4626.14 (±9045.37)	0.060*

CBC = complete blood cell count, Hb = Hemoglobin, RBC = Red blood cell count, PLT = Platelet. CRP = C-reactive protein, NT-proBNP = N-terminal pro b-type natriuretic peptide, PT = A prothrombin time, aPTT = activated partial thromboplastin time, INR = the international normalized ratio.

* $P < 0.05$ for independent sample *t*-test considered statistically significant.

\# Mann-Whiteney was used to calculate *P* value.

that health care providers in SA represented 12.5% of the cases (n = 190). This emphasizes the implementation of strict infection control measures which provided adequate protection within health care setting in SA. In addition, these researchers underlined the importance of early screening for those providers to prevent disease transmission and avoid unnecessary staff depletion.

During the early phase of the COVID-19 epidemic, diagnosing the disease in suspected cases based on symptomatology was increasingly difficult because of the complexity of the symptoms and the similarity with common respiratory infections. Consistent with previous reports [5,9,16], symptoms associated with COVID-19 infection were cough and loss of taste and smell. At the other end of the spectrum, others [17–19] demonstrated that in the vast majority of symptom-manifesting cases, the clinical characteristics of COVID-19 are like those seen in classic SARS-CoV cases. Variations in the main symptomatology were present for fever and cough in Viral Tropism from SARS-CoV, MERS-CoV, and influenza [20].

The most common co-morbid medical conditions were HTN and DM in COVID-19 positive cases, while 54.4% of patients had more than two co-morbid conditions in positive cases group as compared to the COVID-19 negative group. These results were like previous reports [5]. Similarly, HTN, DM, and cardiovascular disease were the most common comorbidities in a meta-analysis of eight studies performed in China with 46,248 patients diagnosed with COVID-19 [21]. Other research [22] also shows that patients with HTN and/or DM exhibit an increased risk of COVID-19 complications, including acute respiratory distress. The mechanism remains under-research, and it is still unclear whether unregulated blood pressure patients have a worse COVID-19 result compared to controlled blood pressure patients.

Since the earliest COVID-19 epidemiological studies were done in China [1], WBC counts emerged as a possible predictor for the risk of COVID-19 infection. The main hematologic findings reported in the current study support this observation. Lymphocytopenia was reported to be associated with a more severe form of COVID-19 [17,23]. Yang et al. provided a plausible explanation for lymphocytopenia in COVID-19 [17]. The group attributes lymphopenia to the destruction of lymphocytes by the virus and subsequent cell death. Notably, lymphocytopenia is also common in patients with Middle East Respiratory Syndromes (MERS) because of lymphocyte apoptosis [24]. Therefore, previous research corroborates the results in this study, indicating that lymphocyte count could be an indicator of disease severity.

Changes in eosinophil counts were not reported in early studies on COVID-19, because of the unclear functions of eosinophils in infections and their relatively small number among WBCs [1,12,19]. However, the current study showed that the number of eosinophils in COVID-19 positive patients was significantly lower compared to the COVID-19 negative group. This might indicate a role for eosinophils, as an early sign of COVID-19 infection. Further research to produce a detailed overview of this mechanism may be necessary. Up to this point, it is hypothesized that the viral assault on bone marrow blocks entry into peripheral circulation of eosinophils, or penetration into certain bodies (such as lungs) [9,25].

A recent study found that although the immune phenotype of COVID-19 is like other coronaviruses, marked differences exist [26]. Severe COVID-19 disease was found to be associated with a decreased number of lymphocytes, eosinophils, and basophils compared to less severe disease. The state of inflammatory cell depletion is strengthened in COVID-19 patients' recovery phase, but this continues or worsens in COVID-19 patients' exacerbated process. They explained the reduced number of peripheral inflammatory cells by the migration of the neutrophils, eosinophils, and lymphocytes from peripheral blood to the lungs, leading to neutropenia, lymphopenia, and blood eosinopenia and concurrent respiratory distress [26]. An increase in peripheral blood inflammatory cells was found to be associated with the outcome of COVID-19. In the study carried out by Sun et al. [26], several points mentioned were significant. Severe type COVID-19 patients have decreased lymphocytes, eosinophils, and basophil counts compared to non-severe COVID-19 patients. The main risk factor for lymphopenia and eosinopenia is a highly severe clinical diagnosis. The state of inflammatory cell depletion is strengthened in COVID-19 patients'

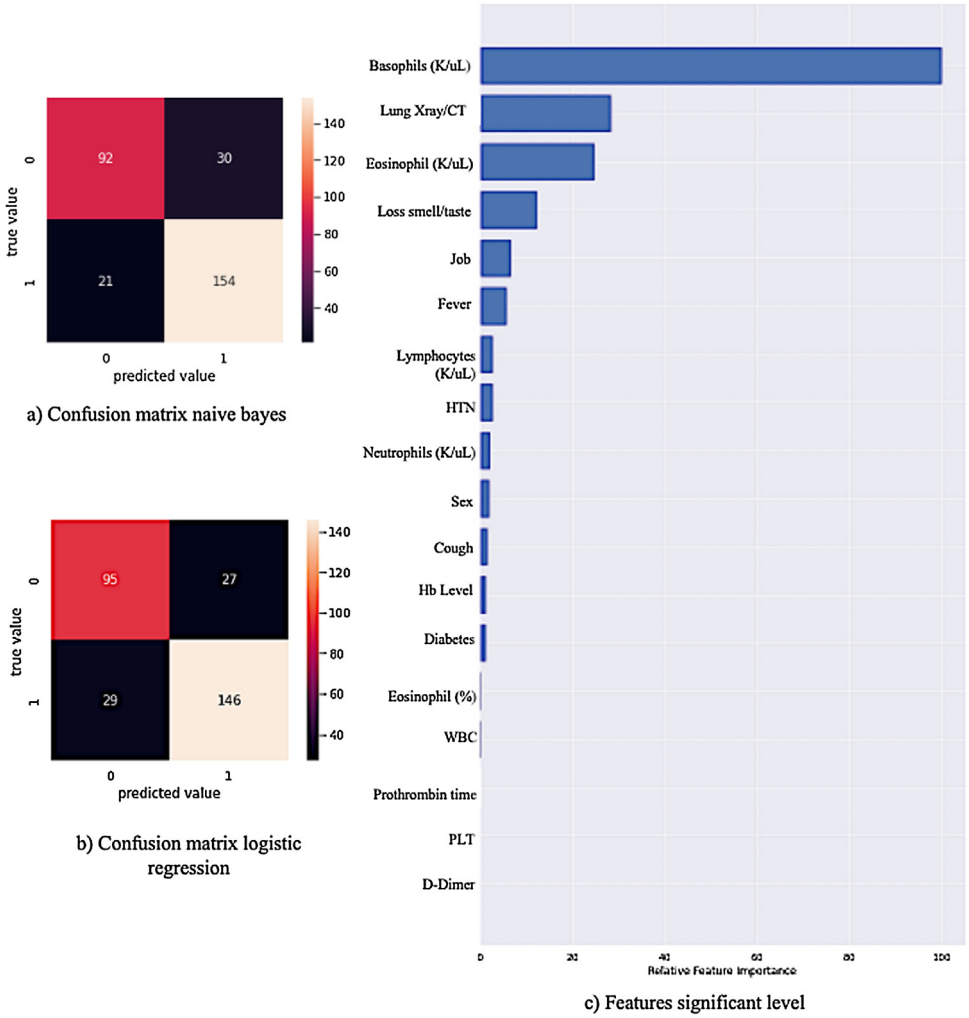

Fig. 2. Machine learning-based diagnosis prediction using confusion matrix of Naive Bayes model (a), and logistic regression model (b). (c) shows the features importance in the logistic regression model.

recovery phase, but this continues or worsens in COVID-19 patients' exacerbated process. They explained the reduction of peripheral inflammatory cells by the migration of the neutrophils, eosinophils, and lymphocytes from peripheral blood to the lungs, leading to neutropenia, lymphopenia, and eosinopenia which led to aggravate respiratory distress [26].

Interestingly, previous studies reported significant changes in various laboratory parameters including lymphopenia, high C reactive protein levels, ferritin, and D-dimer among COVID-19 cases [7,9]. Another study reported significant leukopenia present in around 30% of 24 asymptomatic COVID-19 cases [10]. However, all these were small studies and larger studies are needed to validate those findings.

D-dimers are products of fibrin degradation and have been useful in a clinical decision for the diagnosis of pulmonary embolism, and deep vein thrombosis (DVT) [27]. The association between D-dimer and COVID-19 also was not fully reported with the level changes during disease development. In contrast to earlier findings [28], the present study showed that there was a significantly decreased level of D-dimer in COVID-19 positive patients compared with COVID-19 negative group. However, other variables in this study may contribute to D-dimer findings, as half of the control group have comorbidities and chronic diseases (HTN, DM, heart diseases and malignancy) which influenced D-dimer level.

The D-dimer concentrations decreased concomitantly with inflammation followed by disease improvement, suggesting that it is not possible to produce an estimation of whether anticoagulation is only required in conjunction with D-dimer [28]. This could explain our findings of decreased in the CRP level in COVID-19 positive patients. The diagnostic value of D-dimer levels for thrombus formation in COVID-19 patients is unclear. Tang et al. [29] reported that patients with COVID-19 could have decreased blood viscosity because of high fever and heavy sweating and thus there may be no association with increasing D-dimer levels [29]. D-dimer elevation is not diagnostic of venous thromboembolism and is used mainly as an initial screening test because it has a negative predictive value.

Although group O is the most among ABO groups in the population of this study, as seen in daily practice and in the literature [30], it was less represented in COVID-19 positive patients. This finding was reported in a previous study [31]. Several theories to explain this exist, including a protective effect of anti-A in the serum of group O individuals [32].

One of the most significant findings of this research is to highlight the impact of artificial intelligence in medicine. Artificial intelligence and machine learning techniques could help clinicians efficiently decide, evaluate alternatives, identifying changes, or predict outcomes. In the health care domain, in particular, artificial intelligence techniques can help to emulate human cognition in understanding, analyzing, and interpreting healthcare data such

as patients' health records and medical images. This timely process is especially important in health emergencies and pandemics in controlling the spread of infectious diseases.

Conclusion

There is an urgent need for early diagnosis of COVID-19 and to identify factors associated with worse prognosis. The healthcare sector in SA is going through a major transformation, based on Saudi Vision 2030. The focus of this transformation is to achieve better preparedness and proficiency in dealing with economic changes, globalization, and pandemics while providing excellence in patient care. Artificial intelligence is one of the most important key enablers in this transformation to predict disease outcomes.

Predictors of clinical disease severity in COVID-19 patients and disease progression include lymphopenia. Hematological assessments could, therefore, become a COVID-19 sentinel and deserve consideration in the care process for COVID-19 patients. D-dimer levels in COVID-19 patients are associated with inflammation. Abnormal D-dimer changes and inflammatory factors may show that the treatment with anticoagulants is appropriate.

Authors contribution

Idea development: Dr. Fatmah O Kamel, Dr. Rania. Magadmi.

Study design: Dr. Sulafa T. Alqutub.

Acquiring data: Dr.Fatmah O Kamel, Dr. Rania. Magadmi, Mazen Badawi, Tariq Madni.

Data analysis: Dr. Sulafa T. Alqutub, Dr. Maha Badawi, Dr. Fatin Al-Sayes, Dr.Soheir Adam.

Machine learning analysis: Dr. Areej Alhothali, Dr. Ehab A. Abozinadah.

Drafting the manuscript: Dr.Fatmah O Kamel, Dr. Rania. Magadmi.

Critical revision of the paper: Dr. Sulafa T. Alqutub, Dr. Maha Badawi, Dr. Fat-n Al-Sayes, Mazen Badawi. Dr.Soheir Adam.

All authors read and approved the final manuscript.

Availability of data

Data that support the findings in the current study are available from the corresponding author on reasonable request.

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Competing interests

None declared.

Ethical approval

Not required.

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Appendix A. Supplementary data

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