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Laboratory Findings from 100 Patients with COVID-19 Pneumonia in Madinah, Saudi Arabia

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

The coronavirus disease 2019 (COVID-19) virus, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is spreading rapidly. The purpose of this study is to explore high risk patients and guiding future management and summarize the results of routine laboratory testing of asymptomatic, mild to moderate, severe and critical COVID-19 in order to define practical indicators for the diagnosis and treatment of COVID-19. A total of 100 confirmed COVID-19 patients from Madinah city, Saudi Arabia, hospitalized between March to June, 2020 were included, and categorized into asymptomatic, mild to moderate, severe and critically ill patients. Fasting blood samples were withdrawn from all patients for estimation of complete blood count, coagulation profile, biochemistry and serology. Patients were grouped on the basis of the interval between symptom onset: group 1 (asymptomatic), group 2 (mild to moderate), group 3 (severe), and group 4 (critical). Laboratory features and their distribution were analysed and compared across the four groups. Combining assessment of clinical and laboratory findings could facilitate early diagnosis of COVID-19 pneumonia. Median age was 51 years old and 85% of the patients were men. Overall, all patients were admitted to hospitals and 42% required ICU treatment. The majority of patients (29%) were diagnosed with mild to moderate disease, 28% of patients were critical, 26% of patients were

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severe and 17% of patients were asymptomatic. The comparison COVID-19 patients' four parameters, using Kusakal-Wallis test, showed a significant difference in the levels of lymphocytes, ESR, PT, INR, d-dimer, CK, BUN and ferritin (P <0.05). C-reactive protein greater than 2.97 (0.84-9.18; p<0.0001). The potential risk factors of older age, lymphopenia, d-dimer greater than 1µg/mL and ferritin greater than 500ng/mL could help physicians to identify patients with a poor prognosis at an early stage.

Keywords: COVID-19; Lymphocyte; Ferritin; creatinine kinase; acute respiratory syndrome.

ABBREVIATIONS

COVID-19, Lymphocyte		
ESR	*:*	*Erythrocyte sedimentation rate*
PT	*:*	*Prothrombin time*
D	*:*	*Dimer*
AST	*:*	*Aspartate aminotransferase*
LDH	*:*	*Lactate dehydrogenease*
CK	*:*	*Creatinine kinase*
BUN	*:*	*Blood urea nitrogen*
Ferritin, CRP	*:*	*C-reactive protein*

1. INTRODUCTION

Beginning in December, 2019 a cluster of cases of pneumonia with unknown cause was reported in Wuhan, in the Hubei province of China [1]. On January 7, 2020 a novel coronavirus, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; previously known as 2019-nCoV), was identified as the causative virus by Chinese facilities via deep sequencing analysis of patients' respiratory tract samples [2,3]. SARS-CoV-2 has been shown to infect human respiratory epithelial cells through an interaction between the viral S protein and the angiotensin-converting enzyme 2 receptor on human cells; thus, SARS-CoV-2 possesses a strong capability to infect humans [3].

In most of the initial cases of coronavirus disease 2019 (COVID-19), the disease caused by SARS-CoV-2 was epidemiologically linked to exposure to Wuhan's Huanan seafood market, where wild animals are traded [4,5]. Although the market has been closed since Jan 1, 2020 as part of efforts to contain the outbreak, patients without exposure to the market but with a history of traveling to Wuhan or close physical contact with a patient confirmed to have COVID-19, including health-care workers, have also been identified, suggesting strong human-to-human transmission.

More than 17 million coronavirus cases have been reported globally. Coronavirus disease-2019 was declared pandemic by World Health Organization (WHO) having led to thousands of deaths globally. As of July 29, more than 216 countries have been affected by the COVID-19 disease with over 13, 031,281confirmed cases leading to more than 667,060 deaths [6]. The Ministry of Health have reported 272,590 cases of COVID-19 leading to more than 2816 death in the Saudi Arabia [7].

It is a new infectious disease, which primarily causes infection of the respiratory tract, but also can lead to multiple organs dysfunction, with a most notable damage to the kidney and liver. In this study to explore high risk patients and guiding future management and summarize the results of routine laboratory testing of asymptomatic, mild to moderate, severe and critical COVID-19 in order to define practical indicators for the diagnosis and treatment of COVID-19.

2. MATERIALS AND METHODS

2.1 Study Design and Participants

This retrospective cohort study was performed on 100 patients referred to Ohud Hospital, Madinah city, Saudi Arabia, who agreed to participate in this study. The Ohud Hospital is a 250-bed facility with all specialties. The hospital provides primary and secondary care services for Saudi patients. In the Covid-19 pandemic, the hospital has become an isolation center for the Madinah region. Nasopharyngeal swab was collected from suspected patients by a health care provider. The study included a total of 100 patients divided in four groups: asymptomatic group (17 patients), mild group (29 patients), moderate group (26 patients) and severe group (28 patients).

Data were extracted from the Health Electronic Surveillance Network (HESN) and (oasis) Database. This system contains nasopharyngeal

swab polymerase chain reaction and laboratory data, as well as raw outcome data of COVID-19-positive patients from Medinah city.

2.2 Laboratory Procedures

COVID-19 was diagnosed based on the results of quantitative real time-polymerase chain reaction (RT-PCR) testing, performed at the regional laboratory, of nasopharyngeal swab in accordance with the protocol established by the World Health Organization (WHO). A total of 100 individuals were selected from patients admitted to Ohud Hospital in Medinah, Saudi Arabia. The selection criteria for patients with asymptomatic and symptomatic indications, who complain of high fever >38°C, cough and dyspnoea.

All samples were collected by nurses using standard phlebotomy procedures as described elsewhere. Blood was collected as follows: 10 mL in a plain tube for chemistries and serology, 2 mL in a purple k2-EDTA tube for full blood counts, and 1.8 mL in a sodium citrate tube for coagulation profile and D-dimer. All samples were transported to the main laboratory in temperature-controlled bags maintained at 15–25°C and processed on an average of 6 hours after sampling.

All samples were delivered to the CBAHI certified Ohud laboratory on the day of collection. Processing was completed after specimen verification at the main Laboratory's specimen management section and all samples were analyzed on the day of collection. All samples were entered into the electronic database (Oasis system).

2.3 Definition

Definition was stated according to the Saudi Ministry of health (MOH) protocol for patients suspected of / confirmed with COVID-19. All of the patients included in this study were classified into asymptomatic, mild to moderate, severe and critical based on the results from clinical features and lab results [8].

2.3.1 Asymptomatic

Asymptomatic cases were defined by no symptoms

2.3.2 Mild to moderate

Mild to moderate cases were defined by symptoms with no shortness of breath in high risk patients or symptoms with shortness of breath in high risk patients.

2.3.3 Severe

Severe cases were defined by respiratory rate ≥30/min (adults), blood oxygen saturation ≤93%, PaO2/FiO2 ration <300, lung infiltrates > 50 of the lung field within 24-48 hours.

2.3.4 Critical

Critical cases were defined by acute respiratory distress syndrome (ARDS), sepsis, altered consciousness, multi-organ failure. Criteria for patients at high risk for developing cytokine storm (one or more of the following):

a- Ferritin >300 ug/L with doubling within 24h
b- Ferritin >600 ug/L at presentation and LDH >250
c- Elevated D-dimer (>1 mg/ml)

2.4 Statistical Methods

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 24.0. It was used for calculated frequencies and percentages of all nominal variables. Also, statistics calculated 25^{th} percentile 50^{th} percentile (median), 75^{th} percentile and IQR (Interquartile Range) for different groups (1^{st}, 2^{nd}, 3^{rd} and 4^{th} group) for measurable variables (quantitative variables) of lab results. The Chi-square test was used for comparison between the different groups (1^{st}, 2^{nd}, 3^{rd} and 4^{th} group) with respect to demographic characteristics and to compare haematology, biochemistry, hormone and serology results. Also, the non-parametric Kruskal-Wallis test was used to compare measurable variables of lab results for different groups (1^{st}, 2^{nd}, 3^{rd} and 4^{th} group). Results were considered significant for p-values below 0.05 ($P < 0.05$).

3. RESULTS

100 adult patients were hospitalized in Ohud Hospital, between March 19, 2020 and June 30, 2020 and those who had confirmed COVID-19 pneumonia were retrospectively enrolled in our study.

The median age of the patients enrolled in this study was 51 ± 16 years, ranging from 15 years to 85 years and the age distribution was as follows: 2% (n=2) were age <20, 12% (n=12) between 21-30, 14% (n=14) between 31-40, 21%

(n=21) between 41-50, 21% (n=21) between 51-60, 30% (n=30) were age > 61 and most patients were male 85% (Table 1). The dominant nationality among cases was non-Saudi (55, 55%). No significant differences in age (p=0.410), clinical outcomes (p=0.173) or sex distribution (p=0.629) between groups were identified. The most common symptoms at onset were bronchial asthma 34 of patient, followed by diabetes mellitus and hypertension. Chronic kidney failure occurred in 8 and cardiac disease in 9 of the cases. 42 patients required intensive care unit (ICU) mechanical ventilation and 58 inpatients in ward (Table 1).

Among 100 patients who were admitted and discharged, the median time from illness onset to initiation of treatment were antiviral and antibiotic. There were four groups of patients: 17 patients were asymptomatic (group 1), 29 patients were mild to moderate cases (group 2), 26 patients were severe cases (group 3), and the remaining 28 patients were critical cases (group 4) (Table 2).

Table 1. Clinical characteristic of COVID-19 cases in Madinah

Characteristic	Count	Percent
Age		
<20	2	2 %
21-30	12	12 %
31-40	14	14 %
41-50	21	21 %
51-60	21	21 %
>61	30	30 %
Sex		
Male	85	85 %
Female	15	15 %
Nationality		
Saudi	45	45 %
Non-Saudi	55	55 %
Reported comorbidities		
DM	29	29 %
HTN	26	26 %
Bronchial asthma	34	34 %
Renal failure	8	8 %
Cardiac disease	9	9 %
Clinical outcomes		
ICU	42	42 %
Ward	58	58 %

Mean age for all patients (n=100) was 51.03 (years) and standard deviation (SD) 16.87

Table 2. Clinical characteristics variable of COVID-19 cases in Madinah according to presence of clinical symptoms

Characteristic	Group 1	Group 2	Group 3	Group 4	P-value
Age					
<20	1	0	0	1	0.410
21-30	5	2	3	2	
31-40	3	5	3	3	
41-50	2	5	6	8	
51-60	1	8	8	4	
>61	5	9	6	10	
Sex					
Male	13	26	23	23	0.629
Female	4	3	3	5	
Clinical outcomes					
ICU	5	17	10	10	0.173
Ward	12	12	16	18	

Age, leukocytosis, lymphopenia, anemia, erythrocyte sedimentation rate, prothrombin time, active partial thrombin time, d-dimer, blood urea nitrogen, creatinine, creatinine kinase, lactate dehydrogenase, albumin, ferritin, C-reactive protein were retrieved for cases (Table 3).

The laboratory results of the patient groups were summarized in the Table 3. White blood count per mm^3 had median (IQR) value 7800 (5425-10975) with 69% (n=69) of the cases showing normal counts between 4000-11000 and lymphocytes percentage had median (IQR) value 15.8% (6.5-25.8) with 60% (n=60) of the cases showing less 20%, but the critical patients had lower lymphocytes percentage than the severe patients. There were 87 patients with levels of d-dimer above the reference range (<0.5µg/ml); among those, the proportion of critical patients was higher than other groups. Similarly, higher level of d-dimer and blood urea nitrogen (BUN) were also showed (52, 52%), among those with creatinine level of the cases showing normal range level between 50- 80 (38, 38%), and this difference was also statistically significant (P<0.0001). As shown in Table 3, there was significant difference on cardiac enzymes in the creatinine kinase level (CK) more than 200 between lactate dehydrogenase levels more than 300 (59% versus 38%, P<0.0001). Likewise, in this study, albumin level was lower, between 21-30 (64, 64%, P<0.0001). Serum ferritin levels were at the upper limit of the reference range (30-400ng/mL for males and 15-150 ng/mL). In contrast, ferritin level had median (IQR) level of 958 (408.2-1623) with COVID-19 was higher level between 10001-2000 (36%), and this difference was statistically significant (P<0.0001) (Table 3). The level of C-reactive protein above the reference range (<0.52) for critical patients was higher than that of severe patients.

Table 3. Hematology, biochemistry, hormone and serology results

Characteristic	Count	Percent	P – value
Hematology			
WBC (median, IQR)	7.8 (5.425 – 10.975)		
<4.	7	7 %	< 0.0001
4-11	69	69 %	
>11	24	24 %	
Lymphocytes (median, IQR)	15.8 (6.525 – 25.875)		
<20%	60	60 %	< 0.0001
20-40%	34	34 %	
>40%	6	6 %	
Hemoglobin (median, IQR)	12.3 (10.1075 – 14.2)		
<8	7	7 %	< 0.0001
8-10.99	25	25 %	
11-14	40	40 %	
>14	28	28 %	
ESR (median, IQR)	36.0 (21.0 – 62.0)		
<15	15	15 %	< 0.0001
16-20	9	9 %	
21-30	13	13 %	
31-40	18	18 %	
41-50	12	12 %	
>50	33	33 %	
PT (median, IQR)	13.2 (12.4 – 14.1)		
< 10	1	1 %	< 0.0001
10-12	14	14 %	
12-14	57	57 %	
>14	28	28 %	
INR (median, IQR)	1.13 (1.08 – 1.20)		
< 0.9	1	1 %	< 0.0001
0.9-1.0	8	8 %	
1.01-1.5	89	89 %	

Characteristic	Count	Percent	P – value
>1.6	2	2 %	
APPT (median, IQR)	33.55 (28.725 –37.975)		
< 25	5	5 %	< 0.0001
25-30	28	28 %	
30-35	26	26 %	
>35	41	41 %	
D-Dimer (median, IQR)	1.63 (0.7225 – 3.65)		
<0.5	13	13 %	< 0.0001
0.5-2	52	52 %	
2.01-8	25	25 %	
>9	10	10 %	
Biochemistry			
BUN (median, IQR)	6.8 (4.275 – 15.5)		< 0.0001
< 2.1	1	1 %	
2.1-7.2	52	52 %	
7.3-12.2	17	17 %	
>12.3	30	30 %	
Creatinine (median, IQR)	91.05 (65.6225 – 133.75)		< 0.0001
< 50	5	5 %	
50-80	38	38 %	
81-115	25	25 %	
116-140	10	10 %	
141-160	3	3 %	
>161	19	19 %	
CK (median, IQR)	246.5 (151 – 397)		
< 50	2	2 %	< 0.0001
50-100	12	12 %	
101-150	11	11 %	
151-200	16	16 %	
>200	59	59 %	
LDH (median, IQR)	258 (122 – 367)		
< 101	20	20 %	< 0.0001
101-150	7	7 %	
151-200	13	13 %	
201-300	22	22 %	
>300	38	38 %	
Albumin (median, IQR)	27.55 (24 – 31)		
< 15	2	2 %	< 0.0001
15-20	8	8 %	
21-30	64	64 %	
31-40	26	26 %	
>41	0	0 %	
Hormone Ferritin (median, IQR)	958.55 (408.25 – 1623)		
<200	11	11 %	< 0.0001
201-400	14	14 %	
401-1000	27	27 %	
1001-2000	36	36 %	
>2000	12	12 %	
Serology C-reactive protein (median, IQR)	2.97 (0.8465 – 9.18)		
<0.52	11	11 %	< 0.0001
0.52-10	69	69 %	
11-20	10	10 %	
>20	10	10 %	

**Data are median (IQR) and n (%). p-values were calculated by Chi-square test*

Table 4. Laboratory findings of patients with COVID-19 pneumonia

	Group1 (n = 17)			Group 2 (n = 29)			Group 3 (n = 26)			Group 4 (n = 28)			*P - value
	25th	50th (Median)	75th	25th	50th (Median)	75th	25th	50th (Median)	75th	25th	50th (Median)	75th	
WBC	5.35	8.2	9.55	6.15	8.3	11.235	5.2	7	9.575	5.225	7.1	12.775	0.590
Lymphocytes	18.65	25	38.1	7.25	18.6	28	6.35	12.3	24.625	4.5	11.655	23.3	0.003
Hemoglobin	10.95	12.3	15.45	10.625	12.5	14.3	9.9225	12.445	14.375	9.9	11.7	13.85	0.638
D-DIMER	0.29	0.73	1.68	0.625	1.59	3.2	0.7375	1.67	4.345	1.1925	2.075	7.55	0.007
PT	11.7	12.4	13.7	12.4	13.1	14.1	12.475	13.2	13.65	12.675	13.9	14.55	0.037
INR	1.025	1.08	1.11	1.09	1.13	1.195	1.06	1.13	1.1675	1.1	1.22	1.2975	0.001
APTT	28.8	30.8	33	29.1	34.4	37.1	26.8	34.2	40.125	29.525	34.85	41.05	0.257
ESR	12	18	34	19.5	38	65	23.25	43.5	75	34	39.5	63.5	0.010
AST	24	38	45.5	30.5	41	50	30.5	43	60.25	32.575	41.5	81	0.294
LDH	90	241	333	97	249	325	187	333	516.25	188.75	229	352.25	0.133
CK	122.5	168	219.5	132	201	288	199.75	275	451.25	151.25	351.5	551.75	0.006
BUN	3.25	4.5	6.15	4.35	6.2	15.6	5.575	8.8	19.15	3.75	11.1	31.75	0.006
Creatinine	59.9	86.3	111.5	68.35	91.6	123.5	67.85	94	141.875	65.25	89.75	213.25	0.711
Albumin	26.95	33	37.7	24.5	28	32.6	23.95	27.45	30	21.25	24.4	27.8	< 0.0001
Ferritin	175	453	776.5	335	938	1404	602.75	1237.5	1923.75	667	1253	1992.75	0.002
CRP	0.429	0.7	4.905	0.74	1.64	5.5	1.765	3.85	15.9	2.525	7.955	17.9	< 0.0001

Data are 50th median and IQR. p values were collected by Kruskal – Wallis test

Asymptomatic patients had significantly lower percentages of lymphocytes (25%, p=0.003), d-dimer (0.73µg/dl, p=0.007), prothrombin time and INR, respectively (12.4 sec, p=0.037 and 1.08, p=0.001). In the critical patients, prothrombin time was longer, while APPT showed no statistical difference between the four groups. This study showed elevated erythrocyte sedimentation rate (18, p=0,010), creatinine kinase (168, p=0.006), blood urea nitrogen (4.5, p=0.006), albumin (33, p=<0.0001), and C-reactive protein (0.7, <0.0001). Other laboratory findings did not significantly differ among groups (Table 4).

4. DISCUSSION

The coronavirus is a positive sense RNA virus, enveloped, non-segmented and distributed in humans and other mammals. COVID-19 virus is labeled as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which was previously referred to as 2019-nCoV [9]. Recent researchers on COVID-19 mainly emphasized on the lungs as the main organ affected in the disease, whiles less data is reported regarding the involvement of other organs like kidneys and liver [10].

All patients in this study ranged from 15 to 85 years-old. Among the 54 severe and critical patients, the average age was 51 ± 16 years, with the predominant population in the age group of >60 years. These findings are consistent with those previously reported from other countries, as Indian patients were older, compared to the international average age of 47-62 [11,12,13], at 76 years Italian, Americans, Spanish and British [11]**.** Males were affected more than females (males were 85% of the cases), which was in accordance with the results of other workers [12,13,14,15].

The relationship between the age and severity of disease may be due to more comorbidities and weaker immune systems in older patients. Therefore, people with comorbidities, such as bronchial asthma, diabetes mellitus, hypertension, cardiac disease, and renal failure, appear to have a higher risk for COVID-19. Only 17% of our cases had no symptoms (asymptomatic group), mainly in the 31–40 age. Other associated diseases such as hypertension, diabetes mellitus, bronchial asthma, renal failure and cardiac disease aggravate further seriousness of the disease [16,17,18].

These findings are consistent with those previously reported by other researchers [15,16,17,18]. Similarly, a significant increase in the level of d-dimer, prothrombin time, erythrocyte sedimentation rate, creatinine kinase, blood urea nitrogen, ferritin and C-reactive protein.

Lymphocyte percentage are decreased in COVID-19 patients and it has been shown that severe had median lymphocyte percentage of approximately 11.65%, while asymptomatic had a median percentage of 25%, indicating a strong correlation with disease severity and prognosis [13,19].

In agreement with the findings of Zhou et al. [13], Liu et al. [20] and Han et al. [21], correlation of abnormal coagulation profiles with poor prognosis have been observed (Table 4). Severe group have shown significantly higher levels of plasma d-dimers and prothrombin time compared to asymptomatic group.

Among critical patients, elevated serum ferritin were showed (1253 ng/ml), followed by severe patients (1237 ng/ml), mild to moderate patients (938 ng/ml), and asymptomatic patients (453 ng/ml). These findings are consistent with those previously reported by others [16] indicating that fatalities may be due to hyper-inflammation initiated by the SARS CoV-2 [16].

5. CONCLUSION

A pandemic caused by COVID-19 has created a devastating condition throughout the world claiming more than 715,163 lives so far in about 7 months from January to July 2020. The potential risk factors of older age, lymphopenia, d-dimer more than 1µg/ml and ferritin >500 ug/L could help physician to identify patients with poor prognosis at an early stage.

CONSENT AND ETHICAL APPROVAL

The study lasted from March to June 2020, and it was approved by the General Directorate of Health Affairs in Madinah's (Institutional Review Board-457) ethical committee. A written informed consent and questionnaires for possible risk factors were filled up and taken from each of all women who agreed to participate in the study.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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