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Research Article

Clinical Laboratory and Radiological Findings in COVID-19 Patients with Variable Severity: King Fahad Medical City Experience

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Abstract

Background: Patients with Covid-19 infection can present with varying disease severity in the form of critical, severe, and moderate disease. **Objectives and Methodology:** To assess the significance of clinical laboratory and radiology-based findings in Covid-19 disease severity and their impact on clinical outcome, we performed retrospective analyses using various statistical models, of 412 confirmed Covid-19 patients admitted to our hospital. **Results:** Descriptive stats revealed 160 critical (38.8%), 153 severe (37.1%) and 99 moderate (24%) cases among 195 Saudi (47.3%) and 217 non-Saudi patients (52.7%) with a mean age of 54 years and male: female ratio of 3.5: 1. Major radiological findings included bilateral air space disease and ground glass opacities with or without consolidation. Overall survival was significantly lower in critical and severe compared with moderate patients ($p<0.05$). Poor clinical outcome was observed in the elderly and patients with coexisting co-morbidities. NLR is a unique marker and high CRP, ESR, LDH, Ddimer and ferritin levels are independent predictors of disease severity that show strong association with poor outcome in critical and severe Covid-19 patients. **Conclusion:** Differential Clinical laboratory inflammatory/coagulopathy marker profiles between survivors and non-survivors in Covid-19 patients with variable severity are observed.

Keywords: Coronavirus Covid-19; Acute respiratory distress syndrome; Neutrophil-lymphocyte ratio; C-reactive protein; Lactate dehydrogenase; Erythrocyte sedimentation rate; Shortness of breath

Abbreviations: ARDS: Acute Respiratory Distress Syndrome; NLR: Neutrophil-Lymphocyte Ratio; CRP: C-Reactive Protein; LDH: Lactate Dehydrogenase; ESR: Erythrocyte Sedimentation Rate; SOB: Shortness of Breath

Introduction

Human coronavirus disease, a global public health concern first described in December 2019 and caused by SARS-CoV2 or CoVID-19 manifests with varying degree of signs and symptoms [1,2]. Three major categories of patients with confirmed Covid-19 infection have been recognized: critical patients (~5% of total) requiring life sustaining treatments or procedures, having ARDS, sepsis or septic shock; severe patients (~15% of total) who show signs of pneumonia, severe respiratory distress or oxygen saturation <90%; and non-severe representing both mild and/or moderate cases (~80% of total) who show absence of severe or critical disease signs [3]. Other groups of patients who remain free of any disease during the course of Covid-19 infection called asymptomatic (~17-25%) have also been described [3]. Various factors such as surveillance strategies, therapeutic interventions employed, regional demographics, Covid-19 genotype evolution, and vaccination can be expected to alter Covid-19 severity turnover.

Covid-19 is a highly infectious disease that can lead to fatality. As of January 2023, WHO dashboard (covid19.who.int) shows the number of confirmed deaths reported due to Covid-19 to be 6.8 million globally with a case fatality rate of 0.91%. In Saudi Arabia, the number of deaths due to Covid-19 stands at 9571 (covid19.moh.gov.sa) with a case fatality rate of 1.56%. In China and other countries, a case fatality rate of 4-6% in Covid-19 has been reported [4]. Although vaccination against Covid-19 has had a substantial impact on requirement of hospitalization, disease severity, and mortality rate, uncertainties about their efficacy duration and 'long Covid-19' [5] do highlight the need for the identification of better markers for risk stratification, prognostication and effective treatment modalities. Laboratory and radiology-based findings [6,7] could offer an easy and routinely achievable platform to assess predictive markers of disease severity in Covid-19 infection. This study aims to evaluate the significance of laboratory-based inflammatory markers, neutrophil-lymphocyte ratio, and radiological findings among different disease severity groups of COVID-19 patients admitted to a tertiary-care King Fahad Medical City in Riyadh, Saudi Arabia. To our knowledge, this is the first comprehensive laboratory-based investigation from Saudi Arabia and we believe that retrospective analyses are currently a more feasible and practical approach to study laboratory markers in a large cohort of Covid-19 patients.

Methods

Patients

The full cohort of 412 patients included all those admitted to King Fahad Medical City during the peak of pandemic and confirmed by polymerase chain reaction on nasopharyngeal swabs to be Covid-19 positive. Diagnostic criteria and management of patients was done in accordance with WHO and the Ministry of Health, Kingdom of Saudi Arabia guidelines at that time. All the records of the patients PCR results were handled in the Central Command Centre of the Infection Control and Environmental Health department at KFMC. The Departments of PCLMA, Infection Control and KFMC IRB approved the study. Due to the secondary use of data obtained during routine clinical care without any patient contact or harm, informed consent waiver in accordance with IRB policy was obtained.

Routine serial hematologic, biochemical, immunological and/or radiologic investigations were done at KFMC laboratories (CAP accredited). All the data are stored in the hospital management system (EPIC) in individual patient files. Socio-demographic, laboratory and radiologic data were extracted from the medical records and anonymized. Patients were categorized into various disease severity groups in accordance with WHO severity criteria.

Statistical Analysis Procedure

All categorical variables such as gender, age group, nationality, outcomes and severity presented as frequencies and percentages. Continuous variables age, time (days), WBC, Neutrophil, etc. expressed as either Mean ± SD or Median [IQR] depending on the normality of data. The Kolmogorov-Smirnov test was used to confirm the assumption of normal distribution. If the data was biased, a nonparametric test was used. Pearson chi-square / Fisher's exact test was used to determine significant associations between categorical variables, depending on whether the cell was expected to have an expected frequency of less than 5. One-way ANOVA / Kruskal-Wallis test was used to determine the mean / median significant difference between severity of COVID-19 and factors of the study variables. Overall survival of the patients determined the Kaplan-Meir analysis. A two-sided p-value less than 0.05 was considered statistically significant. All data was entered and analyzed using the SPSS 25 Statistics Package (SPSS Inc., Chicago, Illinois, USA) and MEDCALC software version 20.118.

Results

Patient socio-demographic and clinical characteristics

Table 1 shows the socio-demographic, clinical features and radiological findings of patients based on their categorization into disease severity groups: 160 critical (38.8%) all intubated, 153 severe (37.1%) and 99 moderate (24%) with a mortality of 44%, 19%, and 3%, respectively. Kaplan-Meir analysis of the Overall Survival (OS) showed highly significant lower OS in critical and severe compared with moderate patients (Figure 1a).

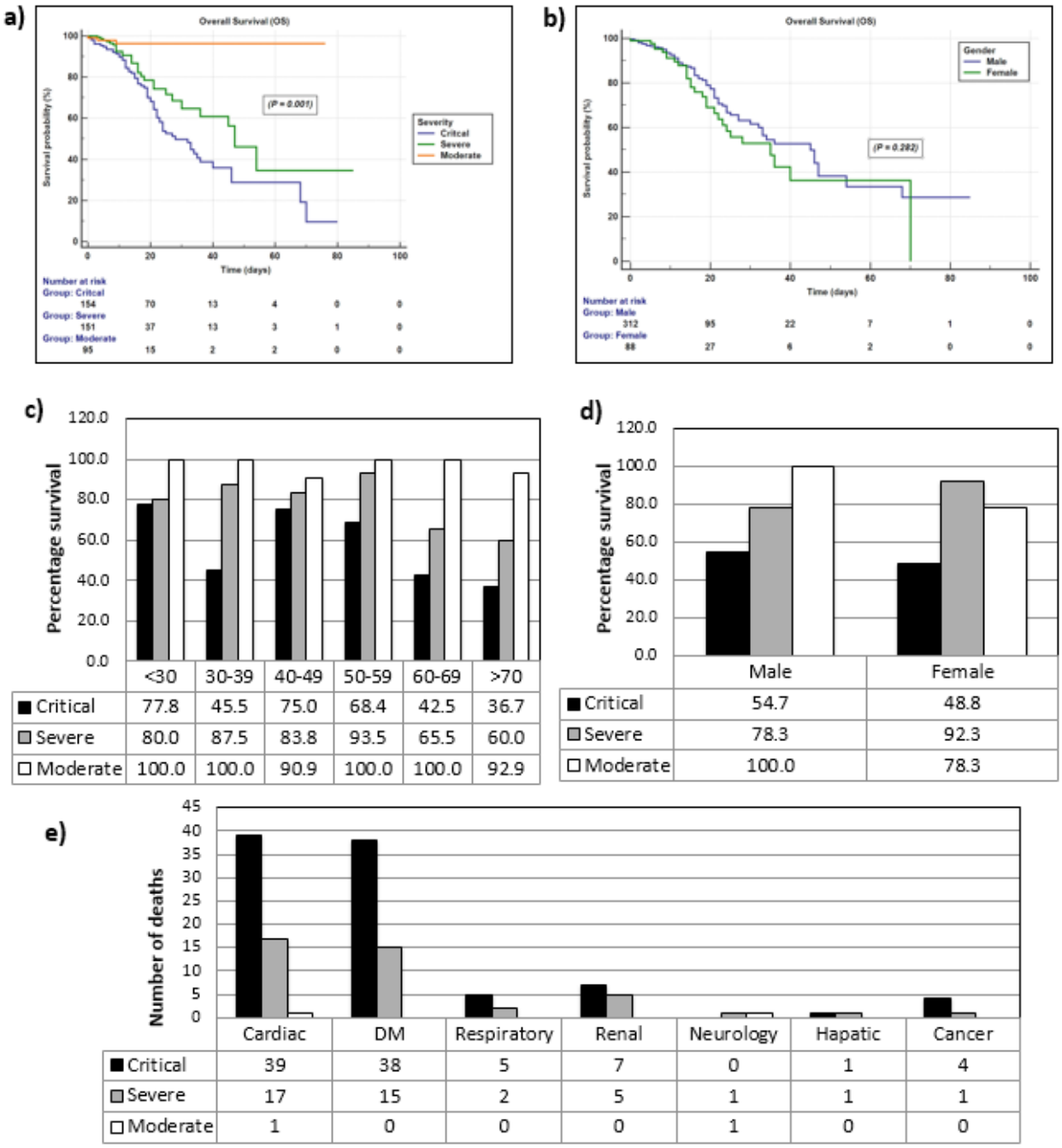

Figure 1: Lower survival of critical/severe compared with moderate Covid-19 patients: percentage probability survival shown by Kaplan-Meier overall survival (OS) curves over a period of 100 days with **a)** disease severity, **b)** gender. The numbers in the bottom show numbers at risk. Percentage survival in disease severity groups with respect to **c)** different age groups, **d)** in male and female gender, and **e)** comorbidity related deaths.

Socio-demographic data and their disease severity distribution shown in Table 1 revealed 195 Saudi (47.3%) and 217 non-Saudi patients (52.7%) with a mean age of 54.7± 14.5 years. Age distribution (<30 to >70 years) revealed majority of the patients over 60 years (44%) and only 19 patients below 30 years (1.3%). Critical (67%) and severe (63%) disease was observed in most patients over 50 years. Gender distribution showed male predominance (77.7% male vs 22.3% females, 3.5:1).

Shortness-Of-Breath, SOB (75.9%), cough (56.8%), fever (49.2%), hypoxia (7%) and chest pain (5%) were major presentation symptoms with the severity distribution shown in Table 1. Other symptoms included viral pneumonia, diarrhea, septic shock, loss of consciousness, tachypnea and only one with known Covid-positive contact.

Variables	**Description**	**Severity**			
		Critical (C)	**Severe (S)**	**Moderate (M)**	**Total**
		(n = 160)	**(n = 153)**	**(n = 99)**	**(n = 412)**
Intubated	Yes	160 (100.0%)	0 (0.0%)	0 (0.0%)	160 (38.8%)
Outcome**	Survived	89 (56.0%)	123 (80.4%)	95 (96.9%)	307 (74.9%)
Nationality	Saudi	67 (41.9%)	76 (49.7%)	52 (52.5%)	195 (47.3%)
	Non-Saudi	93 (58.1%)	77 (50.3%)	47 (47.5%)	217 (52.7%)
Age Group	< 30	9 (5.6%)	5 (3.3%)	5 (5.1%)	19 (1.3%)
	30 - 39	11 (6.9%)	16 (10.5%)	13 (13.1%)	40 (2.7%)
	40 - 49	32 (20.0%)	37 (24.2%)	22 (22.2%)	91 (6.2%)
	50 - 59	38 (23.8%)	46 (30.1%)	21 (21.2%)	105 (7.2%)
	60 - 69	40 (25%)	29 (18.9%)	24 (24.2%)	93 (22.6%)
	≥70	30 (18.8%)	20 (13.1%)	14 (14.1%)	64 (15.6%)
Age	Mean ± SD	56 ± 15	54 ± 14	54 ± 16	54.7 ± 14.5
Gender	Male	117 (73.1%)	130 (85.0%)	73 (73.7%)	320 (77.7%)
	Female	43 (26.9%)	23 (15.0%)	26 (26.3%)	92 (22.3%)

Symptoms	SOB	124 (77.5%)	120 (78.5%)	69 (69.7%)	313 (75.9%)
	Cough	77 (48.1%)	98 (64.1%)	59 (59.5%)	234 (56.8%)
	Fever	69 (43.1)	86 (56.2%)	48 (48.5%)	203 (49.2%)
	Hypoxia	14 (8.7%)	8 (5.2%)	7 (7.5%)	29 (7%)
	Chest pain	3 (1.8%)	8 (5.2%)	10 (10.5%)	21 (5%)
	Viral pneumonia	3 (1.8%)	1 (<1%)	0	4 (<1%)
	Diarrhea	2 (<1%)	1 (<1%)	6 (6.5%)	9 (2.1%)
	Septic shock	2 (<1%)	0	0	2 (<1%)
	ARDS	2 (<1%)	0	0	2 (<1%)
	Abdominal pain	2 (<1%)	3 (<1%)	3 (3.5%)	8 (2%)
	Unconsciousness	2 (<1%)	2 (<1%)	0	4 (<1%)
	Hypothermia	1 (<1%)	0	0	1 (<1%)
	Tachypnea	0	4 (<1%)	1	5 (<1%)
	Sore throat	0	2 (<1%)	0	2 (<1%)
	Covid Positive Contact	0	1 (<1%)	0	1 (<1%)
	Vomiting	0	3 (<1%)	0	3 (<1%)
	Headache	0	0	2 (2.5%)	2 (<1%)
	Loss of smell	0	0	1	1 (<1%)
Radiology	Bilateral air space opacities	125 (78.1%)	119 (77.8%)	86 (86.9%)	330 (80.1%)
	Ground glass opacities with or without consolidation	35 (21.9%)	34 (22.2%)	13 (13.1%)	82 (19.9%)
**highly significant ($p<0.05$)					

Table 1: Socio-demographic and clinical characteristics of Covid-19 patients.

Patient Comorbidity Characteristics

Table 2 shows comorbidities appearing in Covid-19 patients among different severity groups. Patients with coexisting cardiac (36.7%) and diabetic (35.4%) comorbidities were more susceptible to critical (47.5% cardiac and 41.3%, diabetes) and severe (39.2% cardiac, 41.2% diabetes) disease. Immunological, neurological or liver and kidney disease and cancer related comorbidities were equally distributed among severity groups (Table 2).

Comorbidities	**Severity**			
	Critical	**Severe**	**Moderate**	**Total**
	(n = 160)	**(n = 153)**	**(n = 99)**	**(n = 412)**
Cardiac disease	76 (47.5%)	60 (39.2%)	15 (15.2%)	151 (36.7%)
Diabetes mellitus	66 (41.3%)	63 (41.2%)	17 (17.2%)	146 (35.4%)
Immune disease	12 (7.5%)	5 (3.2%)	13 (13.1%)	30 (7.3%)
Kidney disease	8 (5%)	5 (3.2%)	6 (6.6%)	19 (4.6%)
Cancer	5 (3.1%)	1 (<1%)	4 (4.4%)	10 (2.4%)

Neurological disease	2 (1.3%)	4 (2.6%)	3 (3.3%)	9 (2.2%)
Liver disease	2 (1.3%)	1 (<1%)	0	3 (<1%)
Co-morbidities related deaths				
Cardiac disease	39 (51.3%)	17 (28.3%)	1 (6.7%)	57 (37.7%)
Diabetes mellitus	38 (57.5%)	15 (23.8%)	0	53 (36.3%)
Immune disease	5 (41.7%)	2 (40%)	0	7 (23.3%)
Kidney disease	7 (87.5%)	5 (100%)	0	12 (63.2%)
Cancer	4 (32%)	1 (100%)	0	5 (50%)
Neurological disease	0	1 (25%)	1 (33%)	2 (23%)
Liver disease	1 (50%)	1 (100%)	0	2 (66.7%)

Table 2: Co-morbidities distribution and clinical outcome of Covid-19 patients.

Clinical Laboratory Characteristics

Neutrophil-Lymphocyte Ratio (NLR): We collected clinical laboratory data at the time of admission for *hematology markers*: total and differential White Blood Count (WBC), neutrophil and lymphocyte counts, NLR; *biochemical inflammatory markers*: CRP, ESR, LDH, and ferritin; *coagulation markers*: Ddimer, APTT and INR; *liver enzyme levels*: ALT and AST and *cardiac marker* troponin levels (Table 3, Figure 2). Neutrophilia and lymphopenia at presentation was a consistent observation most notable in critical and severe Covid-19 patients analyzed in this study. The mean ±SD neutrophil count (reference range 30-70%) was 81.5 ± 9.4, 80.3 ± 9.1, and 76.3 ± 11.7, and mean lymphocyte count (reference range 23-60%) was 12.1 ± 7.6, 12.6 ± 7.1, and 15.6 ± 8.7 in critical, severe and moderate patients on admission, respectively. We calculated NLR due to its good predictive value on disease severity and mortality in Covid-19 patients, and observed significantly elevated NLR [Median (IQR)] on admission in critical [11.4 (14.7-4.6)], in severe [10.1 (10.9-4.8)] and in moderate [7.1 (8.7-3.4)] cases ($p<0.05$).

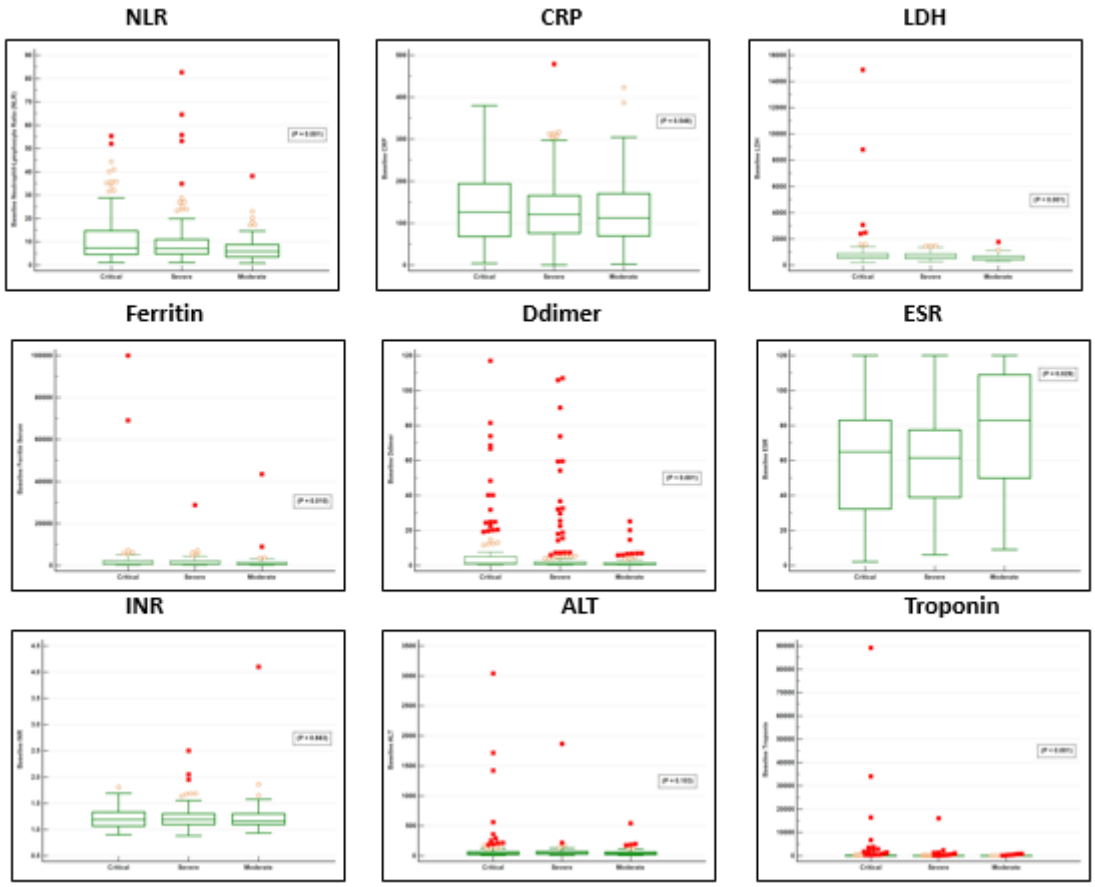

Figure 2: Higher mean laboratory marker levels at presentation in each disease severity group of Covid-19 patients: marker levels on admission for listed analytes. Reference ranges are given in the text and all values are above the range.

Inflammatory markers: On admission we observed increased ESR (reference range 0-20) in critical (60.5 ± 32.3), in severe (59.8 ± 27.9), and in moderate (78.9 ± 31.5) cases; increased CRP (reference range 1-3 mg/L) in critical [126 (193.7-68.2)], in severe [121 (165.7-76.2)], and in moderate [112.5 (171-64.1)] cases; increased LDH (reference range 125-220 U/L) in critical [677 (881-530)], in severe [649 (872-512)], and in moderate [555 (700.5-401.5)] cases; increased ferritin (reference range (10-204 ng/mL) in critical [1149.2 (2406.9-522)], in severe [1042.9 (2213.2-572.1)], and in moderate [729.6 (1664.1-349.5)] cases (Table 3, Figure 2).

Marker on admission	Description	Severity			P - value
		Critical	Severe	Moderate	
WBC	Median [IQR]	10.2 [14.6 - 6.7]	8.7 [11.3 - 6.2]	7.1 [10.1 - 5.4]	*0.001
Neutrophil	Mean ± SD	81.52 ± 9.43	80.33 ± 9.12	76.34 ± 11.76	*<0.001
Lymphocyte	Mean ± SD	12.03 ± 7.64	12.56 ± 7.06	15.59 ± 8.74	*0.001
NLR	Median [IQR]	7.3 [14.76 - 4.66]	7.14 [10.99 - 4.88]	5.86 [8.72 - 3.47]	*0.002
CRP	Median [IQR]	126 [193.75 - 68.18]	121 [165.75 - 76.23]	112.5 [171 - 64.08]	0.546
ESR	Mean ± SD	60.49 ± 32.36	59.81 ± 27.91	78.86 ± 31.48	*0.027
LDH	Median [IQR]	677 [881 - 530]	649 [872 - 512]	555 [700.5 - 401.5]	*<0.001

Ferritin	Median [IQR]	1149.2 [2406.9 - 522]	1042.95 [2213.23 - 572.03]	729.6 [1664.1 - 349.5]	*0.011
Ddimer	Median [IQR]	1.62 [5.03 - 0.78]	1.07 [1.98 - 0.64]	0.85 [1.74 - 0.46]	*<0.001
INR	Mean ± SD	1.22 ± 0.19	1.22 ± 0.2	1.22 ± 0.33	0.938
APTT	Mean ± SD	33.38 ± 15.75	31.45 ± 4.78	31.56 ± 3.92	0.202
AST	Median [IQR]	56 [84.5 - 39.5]	56 [85.5 - 39]	47 [64 - 29]	*0.005
ALT	Median [IQR]	36 [65 - 25]	43 [69 - 30]	35 [60.5 - 22.5]	0.103
Troponin	Median [IQR]	20.7 [94.93 - 6.7]	10.1 [34.05 - 5]	7.4 [16.9 - 4]	*<0.001

Table 3: Laboratory marker distribution in Covid-19 disease severity.

Coagulopathy markers: On admission we observed increased Ddimer (reference range 0-0.5 µg/mL) in critical [1.6 (5.1-0.78)], in severe [1.1 (1.98-0.64)], and in moderate [0.85 (1.74-0.46)] cases; normal APTT (reference range 25.3-38.3 s) in critical 33.4 ± 15.8, in severe 31.5 ± 4.8, and in moderate 31.6 ± 3.9 cases; normal INR (reference range 0.8-1.23 N) in critical 1.2 ± 0.19, in severe 1.22 ± 0.2, and in moderate 1.22 ± 0.33 cases (Table 3, Figure 2).

Liver enzymes and cardiac disease markers: On admission (Table 3, Figure 2) we observed increased AST (reference range 5-34 U/L) in critical [56 (84.5-39.5)], in severe [56 (85.5-39)], and in moderate [47 (64-29)] cases; normal ALT (reference range 0-55 U/L) in critical [36 (65-24)], in severe [43 (69-30)], and in moderate [35 (60.5-22.5)] cases; increased troponin (reference range 0-15.6 ng/L) in only critical cases [20.7 (94.9-6.7)].

Clinical Outcome

The clinical outcome of patients in the form survival (discharge form hospital) or death among disease severity groups is shown with respect to age (Figure 1c), gender (Figure 1d) and comorbidity distribution (Figure 1e). The clinical outcome in relation to various laboratory markers described above is shown (Table 4, Figure 3). The data revealed decreasing survival with increasing age in critical and severe patients (Figure 1c). Majority of the moderate patients survived in all age groups. Survival in females was comparatively lower with more deaths than males but not statistically significant (Figure 1b, 1d). Comorbidities were associated with poor clinical outcome (Table 3). More than half of the critical patients with coexisting cardiac disease and diabetes mellitus did not survive. Fatality was comparatively lesser in severe and moderate patients with these comorbidities (Figure 1e). In moderate patients with a total of three deaths, two had coexisting comorbidities (Table 3, Figure 1e) and the other with age >70 (Table 2, Figure 1c). Critical and severe patients with very high levels of NLR, CRP, LDH, ferritin, and Ddimer had very poor outcome and died than those with normalized values, who survived (Figure 3) suggesting a high predictive value of these markers in Covid-19 infection. It is interesting to note that while elevated ESR was observed on admission among different severity groups, but there was no significant effect on the clinical outcome (Figure 3, ESR panel).

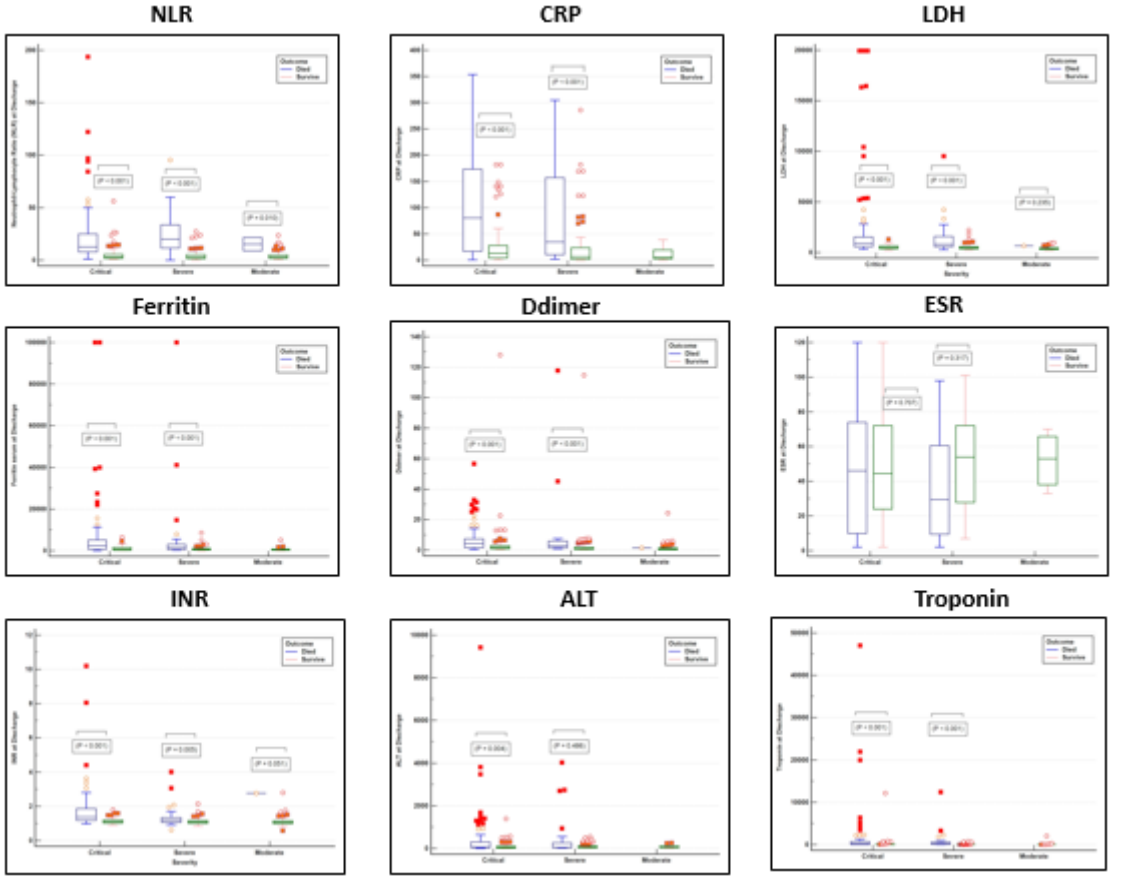

Figure 3: Clinical outcome (survival/death) related to laboratory markers with disease severity in Covid-19 patients: box plot showing Covid-19 related deaths (blue) and survival (green-red) with respect to different laboratory parameters. The data are extrapolated from the values at discharge or before death.

Marker	Description	Critical		Severe		Moderate	
		Survived	Died	Survived	Died	Survived	Died
WBC	Mean ± SD	9.4 ± 5.1	51.8 ± 278.5	8.9 ± 3.8	18.6 ± 10.1	8.4 ± 3.2	14.1 ± 14.2
Neutrophil	Mean ± SD	65.1 ± 15.3	82.8 ± 13.5	67.8 ± 52.4	87.4 ± 9.7	64.7 ± 14.8	84.9 ± 7.4
Lymphocyte	Mean ± SD	23.1 ± 12.1	9.2 ± 8.9	24.3 ± 12.2	6.5 ± 5.8	24.1 ± 11.8	6.6 ± 3.4
NLR	Median [IQR]	2.8 [5.4 - 1.7]	12.7 [24.9 - 7.7]	2.71 [5.3 - 1.7]	19.9 [34.5 - 11.4]	2.9 [4.9 - 1.8]	15.2 [- 8.9]
CRP	Median [IQR]	13.4 [28.4 - 4.1]	80.5 [173.8 - 16.7]	6.5 [23.9 - 1.8]	34.7 [159.5 - 9.9]	5.1 [20.5 - 2.8]	NA
ESR	Mean ± SD	48.4 ± 31.4	48.3 ± 38.8	49.4 ± 28.4	37.4 ± 35.7	52 ± 18.5	NA
LDH	Median [IQR]	459.5 [624 - 372]	880 [1549 - 560]	451 [588.25 - 358.5]	800 [1608 - 569]	359 [455 - 311]	650 [650 - 650]
Ferritin	Median [IQR]	674.3 [1592.5 - 274.6]	2387.6 [5235.9 - 613.1]	607.9 [1030.9 - 361.1]	1405.5 [3282.3 - 574.9]	547.7 [758.4 - 296.1]	NA
Ddimer	Median [IQR]	1.6 [2.9 - 0.9]	4.5 [7.4 - 1.6]	0.9 [1.9 - 0.5]	2.9 [5.9 - 1.5]	0.7 [1.4 - 0.5]	1.5 [1.5 - 1.5]
INR	Mean ± SD	1.1 ± 0.2	1.8 ± 1.5	1.1 ± 0.2	1.4 ± 0.7	1.1 ± 0.3	2.8 ±
APTT	Mean ± SD	32.8 ± 6.1	61.1 ± 45.2	33.6 ± 8.5	51.7 ± 37.9	34.2 ± 17.8	96.4 ±
AST	Median [IQR]	40.5 [56.3 - 22]	67.5 [178.3 - 40]	35 [53.3 - 25.3]	59 [130 - 38.5]	35 [53.5 - 21]	NA
ALT	Median [IQR]	55 [99 - 25]	70.5 [302.3 - 36.5]	67 [100 - 38]	59 [263 - 41]	58 [100 - 41]	NA
Troponin	Median [IQR]	9.1 [34.6 - 4.8]	183.1 [755.9 - 29.6]	4.2 [11.2 - 4]	196.5 [642 - 38.2]	4 [7.8 - 4]	NA

Table 4: Laboratory marker distribution in Covid-19 disease severity.

Radiological findings

Table 1 and Figure 4a and 4b summarize radiological findings Covid-19 patients on admission. Major findings included bilateral air space disease (mild, peripheral, extensive, patchy, and multifocal), and ground glass opacities with or without consolidation.

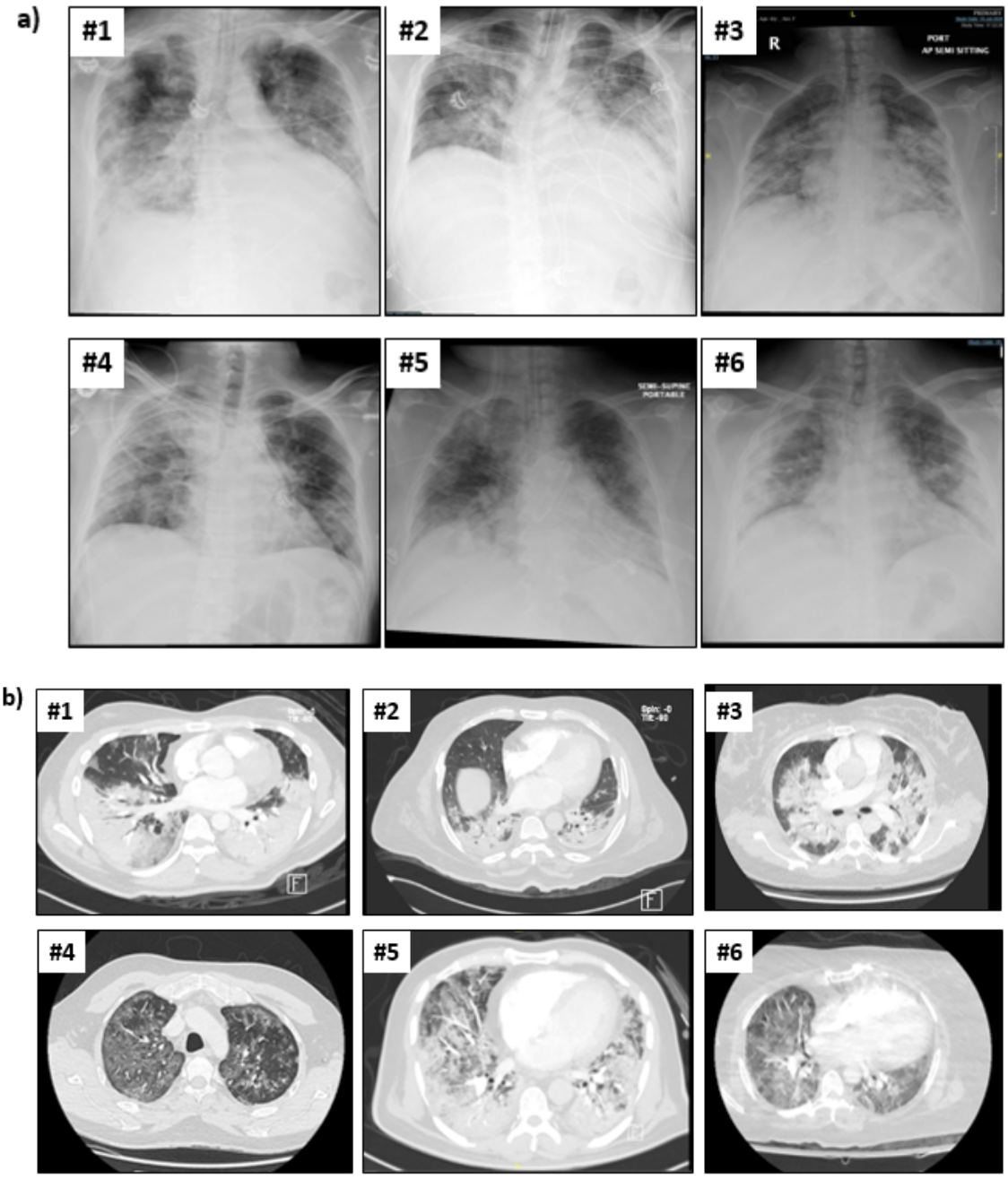

Figure 4: Radiological findings [chest X-ray (a) and CT (b)] on day of admission in Covid-19 patients: a) Portable chest X-ray and **b)** CT chest images in the lung view of representative cases at presentation showing extensive bilateral air space disease (#1, #2), consolidation (#3) and ground glass opacities (#4, #5, #6).

Discussion

The assessment of clinical laboratory-based diagnostic and prognostic markers that have a high predictive value on disease severity and outcome in Covid-19 patients is critical for their effective management, help prevent progression and thus, reduce mortality. We performed retrospective analyses of the socio-demographic, clinical laboratory and radiological features of 412 patients with confirmed Covid-19 infection admitted to our hospital.

We had more critical and severe (76%) than non-severe (24%) Covid-19 cases expected of the medical city in dealing with high-risk patients. In Covid-19, the progression from one severity form to the other may be sudden with even a fatal outcome. Therefore, a clear distinction of the disease severity groups is very essential for various reasons. Frist, non-severe Covid-19 patients may progress to ARDS, septic shock, or multiple organ dysfunction syndrome [8] leading to higher fatality. Second, severe or critical patients have an overall poor prognosis and therefore, their identification early-on is crucial. Importantly, fewer laboratory studies are available that have considered disease severity and clinical outcome. We had significantly higher survival rate in non-severe (97%) followed by severe (81%) and critical patients (56%). In a cohort of 345 patients, Chen R et al. reported the fatality rate of 60% in critical, 34% in severe and 6% in non-severe patients [9]. Consideration of disease severity groups in non-human animal models of Covid-19 should also be taken into account if any similarities are to be drawn.

We had more non-Saudi (52.7%) than Saudi (47.3%) patients. This could just be a coincidence. However, one possible explanation could be that more than a third (~13.5 million) of Saudi's population (35 million) is made up of expatriates from multiple nationalities with various ethnic and linguistic groups from other Arab countries, Asia, Europe, and America (the General Authority for Statistics). Covid-19 can occur in all age groups and age is an important risk factor for the infection. The median patient age was about 55 years with an age distribution below 30 to over 70 years. The percentage survival decreased with increasing age in critical and severe patients and majority of non-severe patients survived in all age groups. Y. Sun, et al. reported the median patient age at 47 years with mild illness in less than 30 years [10]. A meta-analysis in a total of 4663 patients revealed mean age of 48.4 years [4]. A retrospective cohort study found that older age is associated with risk of death [9,11]. Our cohort included more males with significant differences among severity groups and slightly more number of deaths in females than males. Chen R, et al. reported 67% males among all non-survivors, reaching 83% in critical patients [9].

Symptoms on admission and any associated comorbidities are important risk factors in Covid-19 patients. More than half of the critical patients with coexisting cardiac disease and diabetes mellitus did not survive (Table). Symptoms of cough, sputum, and dyspnea were found more common in severe or critical patients, and with non-survivors [9]. Symptoms such as fatigue, anosmia, dyspnea, cough, and myalgia may persist in 'long Covid' [12]. A study by Kompaniyets, et al. showed a higher relative risk for people with complicated diabetes, obesity, and anxiety related disorders (~1.3) and cardiovascular disease (1.1) [13]. A higher risk of adverse Covid-19 outcome that increases with age as seen in our study is estimated to be in about 20% of individuals with chronic conditions [13-15]. A study by Aleanizy FS, et al. also revealed old age, fever, and comorbidities involving diabetes mellitus, asthma, and smoking to be significantly associated with infection severity [16].

We observed higher NLR in critical and severe patients on admission, and in non-survivors compared with survivors. Although lymphopenia and neutrophilia is a prominent finding in most Covid-19 patients [6,17,18], NLR is currently considered as a good predictive marker in disease severity and mortality in Covid-19 patients [19]. Yang, et al. reported elevated NLR to predict prognosis [20]. A meta-analysis by Li X, et al. reported higher NLR of sever patients than mild patients, and also with higher predictive value on mortality [21]. Thus, NLR readily obtained from routine differential CBC analysis could in future, be used as a routine predictive marker in not only Covid-19 infection but also other infections. However, NLR threshold is not clearly defined even in studies that have reported predictive value of NLR on disease severity and mortality. With a larger patient cohort, our study could be used to set up this threshold since comparison of NLR was performed between survivors and non-survivors across all severity groups including the NLR value on admission.

Inflammatory response in all acute infections, with no exception to Covid-19 may be a result of a cytokine storm event [2]. In turn, CRP, ESR, ferritin and LDH levels are elevated as reported by others [22,23]. Abnormal levels of these inflammatory markers could reflect damaged tissues and systemic diseases such as carcinomatosis, collagen vascular disease, sepsis, anemias, thalassemia, chronic liver disease or renal disease. Thus, these markers could be valuable for physicians in assessing these conditions when dealing with Covid-19 patients. Association of these laboratory markers with poor clinical outcome in critical and sever Covdi-19 patients suggests their high predictive value in the se severity groups.

Coagulopathy in terms of Disseminated Intravascular Coagulation (DIC) was reported in Covid-19 patients who died compared with those who survived [24]. We recently reported a CVST case of critical Covid-19 with high Ddimer, who successfully was discharged with preemptive treatment modality. Others have also reported elevated Ddimer in severe than non-sever patients contributing to an array of events with unfavorable

clinical outcome.

Increased liver enzyme and cardiac marker levels in critical and sever patients indicates liver or cardiac-related complications in Covid-19. Viral infection of the bile duct cells or antiviral drug induced liver damage is common in COVID-19 patients [25]. Among patients with COVID-19, there is a high prevalence of cardiovascular disease, and >7% of patients experience myocardial injury from the infection (22% of critically ill patients). Although COVID-19 interacts with the cardiovascular system on multiple levels, increasing morbidity in patients with underlying cardiovascular conditions and provoking myocardial injury and dysfunction [26].

In conclusion, the patients with Covid-19 can experience a range of clinical manifestations with different severity spectrum that may change with age and time. Differential Clinical laboratory marker profiles between survivors and non-survivors in Covid-19 patients with variable severity are observed. The assessment of clinical laboratory-based diagnostic and prognostic markers may provide a simple, rapid, and readily available means of predicting and preventing Covid-19 disease progression, thereby help reduce mortality.

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Authorship List

SM and HS are physicians in Pulmonary Medicine dealing with patients, collected data, and performed clinical characterization of patients.

MSB is a Biostatistician at KFMC Research Center who performed statistical analysis.

AW and FA are physicians who managed and recorded all Covid-19 related cases.

MS and MN are laboratory consultants managing all laboratory data, involved in manuscript editing.

AAPZ collected data, designed the study and wrote the manuscript.

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