



RESEARCH ARTICLE

Association Of Laboratory Abnormalities Before the Beginning of Drug Treatment with Mortality of Hospitalized Patients with Covid-19.

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ABSTRACT

Introduction: Mortality rates of coronavirus disease increased across the world, most patients who hospitalized with covid-19 had good prognosis while a few died. In this study we are going to show that if the Laboratory abnormalities of Renal, Hepatic, Inflammation, Biochemical, Cell blood count, VBG, Cardiac, and Coagulation, before the beginning of drug treatment is death risk factors for COVID-19 patients.

Method: This retrospective cohort study performed on 845 Covid-19 patients, hospitalized in Imam Hossein hospital, Tehran, Iran. Demographic & laboratory were collected by Continuous sampling method from HIS. For data analysis, SPSS 26 software and Chi-square, Fisher's exact, univariable & multivariable logistic regression were used.

Result: Total hospitalized patients were 845 (643 alive, and 202 death). Logistic regression showed that laboratory data such as renal enzyme, Na, Ca, Coagulation, Cell Blood Count, VBG & cardiac enzyme such as CPK, and Troponin were associated with death, while hepatic; Ck-mb, LDH, ESR, CRP, Mg, K, and platelet were not associated.

Conclusion: In this study we found that increased of the level of WBC, BUN, Cr, Na, PT, INR, CPK, & Troponin and decreased of lymphocyte level on admission were associated with increased risk of mortality due to COVID-19 infection and these are most important predictors of mortality in hospitalized COVID-19 patients.

KEYWORDS:

Laboratory abnormalities, radiologic, mortality, covid-19

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INTRODUCTION

Coronavirus Disease 2019 (COVID-19, also known as 2019-nCoV) (1), is an acute respiratory illness with unknown etiology, and highly contagious has been reported in Wuhan, Hubei Province, China since early December 2019 (2-4). International Committee on Taxonomy of Viruses announced that the official classification of the new coronavirus is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). World Health Organization (WHO) pronounced that the official name of this disease caused by the virus is corona virus disease 2019 (COVID-19) (5). In late 2019 WHO declared that this virus disease is a global threat and announced it as a pandemic (6). Mortality rates of coronavirus disease increased across the world (6). Most patients who hospitalized with covid-19 had good prognosis while a few died (7). Few patients have radiographic ground-glass lung changes, abnormal white blood cell, lymphocyte, platelet counts, hypoxemia, alterations in liver chemistries and deranged liver and renal function (8). Previous study confirmed that complications associated with SARS-CoV-2, including acute respiratory distress syndrome (7, 9-11), lower oxygenation index, comorbidities (5), and heart injury (12) were associated with increased mortality. Although many studies declared that laboratory test results associated with severe illness and mortality, the results remain scare (13-15). In this study we are going to show that if the Laboratory abnormalities of Renal, Hepatic, Inflammation, Biochemical, Cell blood count, VBG, Cardiac, and Coagulation, before the beginning of drug treatment are death risk factors for COVID-19 patients.

METHOD

Study design and participants

This retrospective cohort study included adult hospitalized patients (≥ 18 years old) from Imam Hossein Hospital (Tehran, Iran). All adult patients who were diagnosed with COVID-19 base of RT-PCR Covid-19 and chest CT scan were screened and those who died or hospitalized in intensive care unit (ICU) or general ward were included in our study.

Inclusion and exclusion criteria

Inclusions criteria were including age more than 18 years old, definite diagnose of COVID-19 base of positive RT_PCR or chest CT-scan, patient satisfaction to participate in the study and exclusion criteria were including death of the patient for any cause other than Covid-19 and patient satisfaction no to

participate in this study.

Data collection

Demographic and Laboratories test finding and outcome (death/survive) data of patients were extracted from the health information system (HIS) of Imam Hossein hospital and patients clinical document. Laboratory data were checked by two emergency medicine specialist physicians, adjudicated any difference in interpretation between the two primary reviewers.

Clinical & radiologic finding & Laboratories Test

Patient pharyngeal swab specimens were collected for the SARS-CoV-2 viral nucleic acid detection using real-times reverse transcriptase-polymerase chain reaction (RT-PCR) assay. The viral nucleic acid testing for all patients was performed by the clinical laboratory from Imam Hossein Hospital of Shahid Beheshti University of medical science in Iran. Laboratories data were collected at the first day of hospitalization and before the beginning of any drug treatment. The laboratory test data for some patients were missing. Medical radiographic findings, including the chest CT scan, were done for each patient on admission. All medical radiographic finding was generated by the clinical radiographic of Imam Hossein Hospital.

STATISTICAL ANALYSIS

Data were collected by Continuous sampling method. For data analysis, SPSS 26 software and descriptive statistical methods of mean, Chi-square, Fisher's exact tests were used. For explore the association between the laboratories tests and mortality of patient's, univariable, and multivariable logistic regression models were used (16-18). A p-value less than 0.05 were considered as significant.

RESULT

The result showed that total hospitalized patients were 845 (643 alive, and 202 death). Most of patients who hospitalized due to Covid-19 were self-employed (41.2 %), men (58.1 %), married (93.3 %), and more than 65 years (44.1 %), with a mean age of 60.89 ± 17.71 years, ranging from 19 to 91 years. Also, the result showed that most patients who died because of Covid-19 were men (63.9 %), self-employed (42 %), more than 60 years (74.8 %), and married (96 %), with a mean age of 71.86 ± 16.09 years ranging from 43 to 91 years (Table 1).

Table 1: Demographic characteristics of COVID-19 patients.

Variables	Alive case Frequency (Percent) N=643	Death cases Frequency (Percent) N=202	Total cases Frequency (Percent) N=845	P-value
		<i>Gender</i>		
Male	362 (56.3)	129 (63.9)	491 (58.1)	
Female	281 (43.7)	73 (36.1)	354 (41.9)	P = 0.057
Total	643 (76.1)	202 (23.9)	845 (100)	

		Age		
< 45 years	145 (22.6)	18 (8.9)	163 (19.3)	
45 - 65 years	276 (42.9)	33 (16.3)	309 (36.6)	P < 0.001
> 65 years	222 (34.5)	151 (74.8)	373 (44.1)	
		Age Mean		
Year	58.45 ± 17.07	71.86 ± 16.09	60.89 ± 17.71	P < 0.001
		Marital		
Single	49 (7.6)	8 (4)	57 (6.7)	P = 0.07
Married	594 (92.4)	194 (96)	788 (93.3)	
		Job		
Employee	45 (7)	7 (3.5)	52 (6.2)	
Self-employed	270 (42)	78 (8.6)	348 (41.2)	P = 0.061
Housewife	247 (38.4)	73 (36.1)	320 (37.9)	
Retired	81 (12.6)	44 (21.8)	125 (14.8)	

Table 2: Logistic regression between Renal, VBG and Hepatic laboratory data and mortality risk of COVID-19 patients.

Variables	Total cases Frequency N=845	Death cases Frequency (Percent) N=202	B	S.E	Logistic Wald	regression 95%CI	P-value
<i>Renal</i>							
		<i>BUN</i>					
Normal	434	61 (14.05)	-1.173	0.173	45.758	0.22-0.43	< 0.001
Abnormal	402	139 (34.57)					
		<i>Creatinine</i>					
Normal	602	113 (18.8)					
Abnormal	234	87 (37.2)	-0.940	0.171	30.298	0.27-0.54	< 0.001
<i>Vein blood gas</i>							
		<i>VBG</i>					
Normal	379	81 (21.4)	-0.255	0.164	2.418	0.56-1.06	0.012
Abnormal	466	121 (26)					
<i>Hepatic</i>							
		<i>ALT</i>					
Normal	508	129 (25.4)	0.331	0.197	2.834	0.94-2.04	0.092
Abnormal	224	44 (19.6)					
		<i>AST</i>					
Normal	395	83 (21)	-0.315	0.174	3.254	0.51-1.02	0.071
Abnormal	337	90 (26.7)					
		<i>ALK</i>					
Normal	574	132 (23)	-0.008	0.228	0.001	0.63-1.5	0.973
Abnormal	134	31 (23.1)					

The results showed that 34.57% of patients who had abnormal BUN, 37.2% of patients with abnormal Creatinine and, 26% of patients who had abnormal VBG, have died. While most of patients who had abnormal hepatic enzymes such as AST,

ALT, ALK remained alive. Logistic regression showed that the renal and VBG laboratory data were associated with death, while hepatic laboratory data was not associated (Table 2).

Table 3: Logistic regression between Biochemical, Cell Blood Count, and Coagulation laboratory data and mortality risk of COVID-19 patients.

Variables	Total cases Frequency N=845	Death cases Frequency (Percent) N=202	B	S.E	Logistic Wald	regression 95%CI	P-value
Biochemical							
		Na					
Normal	582	118 (20.3)	-0.657	0.171	14.771	0.37-0.72	< 0.001
Abnormal	243	80 (32.9)					
		K					
Normal	497	127 (25.6)					

Abnormal	330	71 (21.5)	0.225	0.169	1.772	0.89-1.74	0.183
		Ca					
Normal	151	29 (19.2)					
Abnormal	409	123 (30.1)	-0.593	0.233	6.474	0.35-0.87	0.011
		Mg					
Normal	402	99 (24.6)					
Abnormal	159	46 (28.9)	-0.220	0.210	1.099	0.53-1.21	0.295
Cell Blood Count							
		WBC					
Normal	504	116 (23)	-0.120	0.164	0.543	0.64-1.22	0.041
Abnormal	341	128 (37.5)					
		Neutrophil					
Normal	274	41 (15)	-0.822	0.193	18.094	0.30-0.64	< 0.001
Abnormal	563	161 (28.6)					
		Lymphocyte					
Normal	268	38 (14.2)	-0.892	0.198	20.268	0.27-0.60	< 0.001
Abnormal	571	164 (28.7)					
		Platelet					
Normal	686	162 (23.6)	-0.407	0.347	1.370	0.33-1.31	0.242
Abnormal	41	13 (31.7)					
Coagulation							
		PT					
Normal	620	133 (21.5)	-0.816	0.219	13.849	0.28-0.68	< 0.001
Abnormal	110	42 (38.2)					
		PTT					
Normal	686	162 (23.6)	-0.407	0.347	1.370	0.33-1.31	0.242
Abnormal	41	13 (31.7)					
		INR					
Normal	595	122 (20.5)	-0.865	0.208	17.307	0.28-0.63	< 0.001
Abnormal	129	49 (38.0)					

The results showed that 32.9% of patients who had abnormal Na, 30.1% of patients with abnormal Ca, 28.6% of patients with abnormal neutrophil, 28.7% of patients with abnormal lymphocyte, 37.5% of patients with abnormal WBC, 38.2% of patients with abnormal PT and, 38% of patients who had abnormal INR, have died. While most of patients who had K,

platelet, Mg, and PTT abnormalities, remained alive. Logistic regression showed that, Na, Ca, Coagulation and Cell Blood Count laboratory data were associated with death, while Mg, K and, platelet laboratory data were not associated (Table 3).

Table 4: Logistic regression between Cardiac, and Inflammation laboratory data and mortality risk of COVID-19 patients.

Variables	Total cases Frequency N=845	Death cases Frequency (Percent) N=202	B	S.E	Logistic Wald	regression 95%CI	P-value
Cardiac							
		CPK					
Normal	449	92 (20.5)	-0.663	0.175	14.302	0.36-0.72	< 0.001
Abnormal	264	88 (33.3)					
		Ck - mb					
Normal	387	87 (22.5)					
Abnormal	134	35 (26.1)	0.198	0.231	0.734	0.77-1.91	0.392
		Troponin					
Normal	544	110 (20.2)	1.085	0.237	20.918	1.85-4.71	< 0.001
Abnormal	91	39 (42.9)					
		LDH					
Normal	94	16 (17.0)	-0.375	0.299	1.567	0.38-1.23	0.211
Abnormal	396	91 (23.0)					
Inflammation							
		ESR					

Normal	56	11 (19.6)	0.334	0.350	0.909	0.70-2.77	0.340
Abnormal	566	144 (25.4)					
		CRP					
Normal	30	6 (20.0)	0.235	0.465	0.255	0.50-3.14	0.614
Abnormal	691	166 (24.0)					

The results showed that 42.9% of patients with abnormal Troponin, and 33.3% of patients who had abnormal CPK, have died. While most of patients who had Ck-mb, LDH, ESR, and CRP abnormalities, remained alive. Logistic regression showed that cardiac enzyme such as CPK, and Troponin were associated with death, while Ck-mb, LDH, ESR, and CRP laboratory data were not associated (Table 4).

DISCUSSION

This study provides robust evidence about the prevalence, pattern, severity, and dynamic changes in Laboratory abnormalities, as well as associated clinical outcomes and mortality, in patients with COVID-19 in Iran. Results showed that about 24 percent of patients who participated in this study were died, previous study conformed this finding. Wenjie Tian & et. al in a systematic review study including 14 study that performed on predictors of mortality in hospitalized COVID - 19 patients reported that a quarter of hospitalized Patients with COVID - 19 died (6), which is higher than previously reported (19), They also reported that baseline cardio metabolic disease and evidence of increased acute inflammation and end - organ damage (cardiac, renal, liver, and hematologic) on admission were associated with increased risk of mortality due to COVID - 19 infection (6) that is consistent with our study.

Results in this study showed that Liver laboratory abnormalities including ALT, AST and ALK were not associated with mortality of patient with COVID-19. Ding & et.al reported that Abnormal liver laboratory at admission were independent predictors of COVID-19 mortality. Therefore, monitoring liver chemistries, especially Abnormal liver laboratory, in hospitalized patients with COVID-19, is necessary (20). The prevalence and prognostic value of abnormal liver chemistries in COVID-19 varies across different studies (21, 22) and are influenced by the baseline characteristics of patients such as age, severity of pneumonia, pre-existing comorbidities, and the presence of multi organ failure.

Logistic regression showed that inflammatory markers such as ESR, and CRP were not associated with mortality of covid-19 patients in contrast with our study a systematic review study reported that inflammatory markers, such as CRP and ESR, were also observed in the nonsurvival group (6). Result also showed that cardiac enzyme such as CPK, and Troponin were associated with death of Covid-19 patents, this finding approved by previous study (12, 23-25).

In the current study, levels of BUN and Creatinine were indicative of abnormal kidney function at the time of

admission in non survivors compared with survivors and they were associated with mortality, previous study approved this finding (6). Tian & his colleague in their systematic review study with review of other clinical trial study reported that mortality of covid-19 patents is associated with lower platelet count and elevated PT & INR levels, suggesting a possible coagulopathy. in these patients also we observed that patients in the dead group were more likely to have a higher WBC count and lower lymphocyte (6). This finding is in consistent with present study, in our study result showed that elevated of PT, INR & Cell Blood Count level and lower lymphocyte were associated with mortality but platelet was not associated that is in contrast with their study.

CONCLUSION

In this study we found that increased of the level of WBC, BUN, Cr, Na, PT, INR, CPK, & Troponin and decreased of lymphocyte level on admission were associated with increased risk of mortality due to COVID - 19 infection and these are most important predictors of mortality in hospitalized COVID - 19 patients. These findings suggest that initial laboratory assessment is important for risk stratification of patients with COVID - 19 and that those demonstrating markers of end - organ dysfunction, inflammation, or coagulopathy are at increased risk of a poor outcome.

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CONFLICTS OF INTEREST

There are no conflicts of interest

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