



BIOCHEMICAL AND HEMATOLOGICAL PARAMETERS AS PROGNOSTIC MARKERS IN COVID-19 PATIENTS

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Abstract:

This study aims to investigate the alteration in biochemical and hematological parameters in Covid-19 patients. Total 200 patients were randomly selected during their hospitalization in Holy family Hospital Rawalpindi, Pakistan. The patients were then categorized as severe and non-severe group as per criteria provided by WHO and nasal swabs for qPCR analysis and blood sample were subjected to biochemical and hematological profiles. The data was then subjected to statistical analysis using SPSS 24.0. Out of 200 patients, 49% (98) were females and 51% (102) were males. The mean age was of the study population was 52.45 years. The most frequent sign and symptoms were, cough, fever and shortness of breath. About 59.5 % (119) patients were categorized in severe group and 40.5% (81) were non-severe. The overall mortality was 21.0% (42) within hospital (mean stay at hospital 6.68 days). The most frequent comorbidities were HTN (37.5%), DM (33.5%) and IHD (13.5%). Among liver function test total bilirubin was found to be independent predictor for mortality (OR=2.517 C. I. 1.428-4.438) with p-value (0.001). The Odds ratio for urea and creatinine (OR=6.407 C. I 2.188-18.763) respectively. Among electrolytes chloride having the Odd ratio (2.536 C. I 1.189 5.405 with p-value 0.016) was found independent mortality predictor. In coagulation markers PT (OR= 3.722 C. I 1.018-13.610, p-value 0.047) and for APTT (OR=4.873 C. I 1.856-12.794 p-value 0.001) were independent predictor of mortality. Lastly, among hematological parameters TLC (OR=4.004 C. I 1.816-8.827, p-value 0.001), neutrophil count (OR=4.148 C. I 1.320-13.033, p-value 0.015) and NLR (OR=2.081 C. I 1.388-3.120, p-value <0.001). This study demonstrates the association of various comorbidities, biochemical and hematological parameters with Covid-19 severity and mortality. Hypertension, diabetes mellitus, ischemic heart diseases and advance age were significantly associated with severe Covid-19 infection. ALT, total bilirubin, urea, creatinine prothrombin time and APTT was significantly increased in severe patients. Hyponatremia was

profound in deceased patients and hypochloremia was profound in severe Covid-19 cases. Leukocytosis, neutrophilia, thrombocytopenia and NLR were also associated with severe Covid-19 infection.

Keywords: Prothrombin time, Activated partial thromboplastin time, Leukocytosis, hyponatremia

Introduction

Severe acute respiratory syndrome coronavirus-2 is a novel Corona virus that emerged in China, in December, 2019 and caused worldwide health crisis and approximately 6.9 million deaths. Sars-CoV2 belongs to *Betacoronavirus* genus and has the capability to invade human cells and cause infection (1). The SRAS-CoV2 is an enveloped virus, has a single standard, non-segmented positive sense RNA genome 29.8 to 29.9 kb which contains 12 ORFs and encodes 16 non-structural proteins, 4 structural proteins and 9 accessory proteins. The four major structural proteins are Nucleocapsid (N), envelope (E), membrane (M) and spike protein (S) which mediate host cell and viral interactions (2).

The primary mode of transmission of human coronaviruses is through respiratory droplets, meanwhile the other modes for example air borne droplets, transmission via contaminated surfaces, oral-fecal transmission also has been reported (3). SARS-CoV2 gains entry into host cells which is mediated by Spike glycoprotein which binds to ACE2 receptors and multiple in the upper respiratory tract; multinucleated cells of nasopharynx and trachea and sustentacular cells in nasal olfactory mucosa. The virus can disseminate in the lower respiratory tract if not contained resulting in alveolar infection (4). The symptoms include cough, flu, sore throat, loss of smell, loss of taste, generalized body pain and fever. The disease exhibits a wide range of symptoms, from asymptomatic to severe multi-organ failure which has led to a high rate of morbidity and mortality. The mortality risk increases with age and people suffering from other co-current chronic diseases i.e., cardiovascular diseases, pulmonary infections, diabetes mellitus and renal issues (5).

Two major pathological features of Covid-19 are diffuse alveolar damage and hyperactivation of the coagulation cascade which leads to a hyper-inflammatory state (6). The virus then disseminates to the vasculo-endothelial system and major body organs liver, kidneys and heart having ACE2 receptors and can cause severe damage either by direct infection, hypoxia, due to T-cell mediated cytotoxicity and due to hyper-inflammatory response "cytokine storm" (7).

The high mortality rate within hospital settings remained a serious concern. In this regard, biochemical and hematological parameters play a crucial role in terms of disease prognosis and outcome as they are the reflex of damage to organs liver (8), kidneys (9), immune and coagulation system hyperactivation (10,11).

This study is aimed to delineate the significance of these biomarkers to assess the severity of Covid-19 in hospitalized patients especially with advanced age and various comorbidities. In this study total 200 patients were randomly selected from Holy Family Hospital Rawalpindi, Pakistan and categorized into severe and non-severe groups. The demographic data, clinical history of co-existing diseases and duration of hospitalization was collected from both groups. Followed by collection of Nasal swabs which were subjected to qPCR analysis for confirmation of Sars-CoV2 positive cases. Confirmed positive patients then included in study and their blood samples for biochemical and hematological profiles were collected. The results of these profiles then compiled and subjected to rigorous statistical analysis.

Materials and Methods

The ethical approval for the recruitment of human subjects and for various sample collection, requirement of all necessary clinical history and personal information was taken from the Ethical Committee of PMAS Arid Agriculture University Rawalpindi, Pakistan and from Institutional Research and Ethics Forum Rawalpindi Medical University and Allied Hospitals Rawalpindi, Pakistan.

Exclusion Criteria

Patients who were receiving any antiviral therapy, blood thinner medication like warfarin, loprin,

autoimmune disorders, autoimmune hepatitis, idiopathic thrombocytopenia, dengue hemorrhagic fever, any major surgeries and pregnant women were also excluded.

Inclusion Criteria

Only SARS-COV-2 positive patient diagnosed by RT-PCR were included. Patient above 18 years male or females with diabetes mellitus, hypertension, cardiovascular diseases, asthma, pulmonary tuberculosis, chronic obstructive pulmonary diseases, obesity, chronic kidney disease were also included in the study.

Study variables:

Besides the comorbidities and demographics, urea, creatinine, sodium, potassium, chloride, total bilirubin, alanine aminotransaminase, alkaline transaminase as biochemical variables whereas, hematological variables include, total leukocyte count, platelet count, Neutrophil count and lymphocytes count and coagulation markers include prothrombin time and activated partial thromboplastin time.

Sample Collection:

The nasopharyngeal swabs, oral swabs were collected in 3ml of universal viral transport medium (DNA/RNA preservation kit) for qPCR analysis. For hematological analysis and blood counts the whole blood samples were collected in 3ml Ethylene diamine tetra-acetic acid with di-potassium (EDTA-k₂), biochemical profiling 3ml blood collected into clot activator vials and for coagulation studies blood samples were collected in tri-sodium citrates tubes.

Materials and instruments used:

For personal protective measure, N95 masks, goggles for eyes protection, disposable overalls, DNase and RNase free nitrile gloves, pipettes of 1000 ul, 100 ul and 10 ul with disposable filtered tips used and 70% ethanol was used to decontaminate lab surfaces, instruments and apparatus. For Nucleic acid extraction semiautomated extractor by bioperfectus technologies SMPE-960 used which principle is based on magnetic beads mediated nucleic acid extraction. For amplification of extracted nucleic acid real time system, CFX96™ Real-Time PCR System made by BIO-RAD was used.

Biochemical and hematological analysis:

For biochemical analysis Beckman Coulter AU680 total lab automation system was used in local facility The whole blood analysis for complete blood picture was performed on Mindary-Bc 5000 a five-port automated hematological analyzer and coagulation studies were conducted on automated coagulation analyzer sysmex CA-660.

Statistical analysis:

For demographics and comorbidities chi-square analysis was applied. Quantitative variables were subjected for normal distribution first then non-parametric variable subjected to Man-Whitney U test and parametric data was analyzed by ANOVA. Significantly different parameters then subjected to receiver operator curve (ROC), binary logistic regression and finally Kaplan Meier survival analysis using SPSS 24.0.

Results

Baseline Characteristics

There were 200 hundred patients recruited in this study, 98 (49%) patients were females and 102 (51%) were men. The mean age was 52.45 years with a standard deviation of ± 15.50 , The minimum and maximum age 24 and 95 years respectively. The incidence of hospitalization was 8.5% (n=17) in age group 20-29, 30-39 years it was 14.0% (n=28), among 40-49 years incidence was 18.0% (n=36), in age group 50-59 the incidence of admission was calculated 21.5% (n=43), the age group 60-69 years, 69-79 years and ≥ 80 years the incidence of hospitalization was, 21.0% (n=42), 13.5% (n=27) and

4.0% (n=8) respectively.

Out of 200 patients 80.5% (n=161) had fever and cough, ageusia wa0073 found in 5.0% (n=10), the complaint of anosmia was found in 5.5% (n=11) patients, dyspnea in 2.0% (n=4), 3.0% (n=4) patient had symptoms of flu headaches and Bodyaches reported in 0.5% (n=1) and 3.5% (n=7) respectively and lastly shortness of breath was reported by 81.0% (n=162).

Out of 200 patients 81 (40.5%) were placed in Non-severe group and 119 (59.5%) patients were in severe. Whereas, 158 (79.0%) patients discharged as survivors and 42 (21.0%). Table#1 presents the details of various comorbidities across the gender, severe, non-severe and expired patients with their statistical significance (chi-square test). The other less frequent and statistically not significant comorbidities were chronic pulmonary obstructive diseases (n=2), acute kidney injury (n=1), asthma (n=10), tuberculosis (n=5), chronic kidney disease (8) and chronic hepatitis C (2).

Cases	Age groups							Gender		Group		Outcome		P Value	
	19-29	30-39	40-49	50-59	60-69	70-79	≥80	M	F	Severe	Non-Severe	Discharged	Expired		
DM	67 (33.5%)	NIL	4 (5.97%)	12 (17.9%)	16 (23.8%)	25 (37.3%)	8 (11.9%)	2 (2.98%)	25 (37.3%)	42 (62.6%)	34 (50.7%)	33 (49.2%)	51 (76.1%)	16 (23.8%)	0.04
HTN	75 (37.5%)	NIL	3 (4.0%)	14 (18.6%)	19 (25.3%)	23 (30.6%)	16 (21.3%)	NIL	31 (41.3%)	44 (58.6%)	55 (73.3%)	20 (26.6%)	52 (69.3%)	23 (30.6%)	0.001
IHD	27 (13.5%)	NIL	NIL	NIL	7 (25.9%)	11 (40.7%)	8 (29.6%)	1 (3.7%)	20 (74.0%)	7 (25.9%)	22 (81.4%)	5 (18.5%)	17 (62.9%)	10 (37.5%)	0.001

Table 1: Summary of most frequent and significantly different comorbidities among Covid-19 patients

Association of Biochemical markers with Covid-19 severity

Among LFTs the means of total bilirubin and alanine aminotransferase were found to be statistically different among severe and non-severe groups with a (p=0.007 at 95% CI) and (p=0.003 at 95% CI) respectively Table No 2. In severe patients 21.8% have increased total bilirubin, ALT was raised in 50.4% patients and ALP was raised in 36.1% of severe patients.

Biochemical Markers

Parameters	Severe			Total	Non-Severe			Total	Expired			Total	P value
	Low	Normal	High		Low	Normal	High		Low	Normal	High		
Total bilirubin	2 (1.68%)	91 (76.4%)	26 (21.8%)	119	7 (8.64%)	65 (80.2%)	9 (11.1%)	81	1 (2.38%)	28 (66.6%)	13 (30.9%)	42	**0.007
ALT (Male)	NIL	25 (40.9%)	36 (59.0%)		NIL	27 (65.8%)	14 (34.1%)		NIL	13 (61.9%)	8 (38.0%)		**0.014
ALT (Female)	NIL	34 (58.6%)	24 (41.3%)		NIL	30 (75.0%)	10 (25.0%)		NIL	14 (66.6%)	7 (33.3%)		0.071
ALP	1 (0.84%)	75 (63.0%)	43 (36.1%)		NIL	60 (74.0%)	21 (25.9%)		NIL	28 (66.6%)	14 (33.3%)		**0.944
Urea	2 (1.68%)	40 (33.6%)	77 (64.7%)		1 (1.23%)	69 (85.1%)	11 (13.5%)		NIL	6 (14.2%)	36 (85.7%)		**<0.001
Creatinine	NIL	67 (56.3%)	52 (43.6%)		NIL	69 (85.1%)	12 (14.8%)		NIL	14 (33.3%)	28 (66.6%)		**<0.001
Sodium	39 (19.5%)	67 (56.3%)	13 (10.9%)		13 (16.0%)	68 (83.9%)	NIL		9 (21.4%)	23 (54.7%)	10 (23.8%)		**<0.001
Potassium	27 (22.6%)	73 (61.3%)	19 (15.9%)		4 (4.93%)	69 (85.1%)	8 (9.87%)		12 (28.5%)	24 (57.1%)	6 (14.2%)		0.398
Chloride	31 (26.0%)	68 (57.1%)	20 (16.8%)		16 (19.7%)	62 (76.5%)	3 (3.70%)		7 (16.6%)	22 (52.3%)	13 (30.9%)		**0.001

Table 2: Distribution of biochemical parameters in Covid-19 patients.

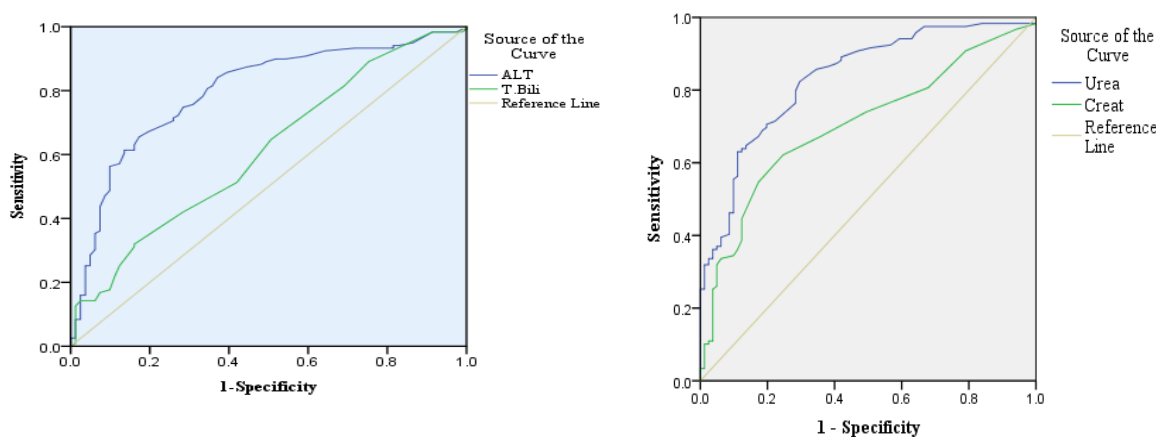
To further determine the extent of liver damage the classes of upper limit of normal (ULN) formulated for ALT. The cut off value for the 1 ULN of ALT for male and female determined ≤ 40 U/l and ≤ 30 U/l respectively (12). 22 Out of 46 severe male patients had alanine aminotransferase in 1ULN (≤ 40), 27 patients had ALT in 2 ULN (41-80), 4 patients had ALT levels in 3 ULN (81-120) and 4 ULN (121-160) class, 3 patients had ALT levels in 5 ULN (161-200) and 1 patient had ALT levels >5 ULN (>200). In female patients of severe Covid-19, 26 observations were found in 1 ULN (≤ 30) class, 17 were in 2 ULN (31-60) class, 10 patients had ALT levels in 3 ULN (61-90), 4 patients had ALT levels in 4 ULN (91-120) class and 1 patient had ALT levels in >5 ULN (>200) class

In renal function tests the severe Covid-19 patients 64.7% have increased urea and 43.6% have increased creatinine levels. Among 42 mortalities 36 patients have increased urea and 28 patients have increased creatinine levels. The difference in distribution of urea and creatinine in severe and non-severe patients was statistically significant ($p < 0.001$).

The distribution of electrolytes in severe patients, hyponatremia was profound in 19.5%, hypokalemia 22.6% and hypochloremia was seen in 26.0%. whereas, hypernatremia was seen in 10.9%, hyperkalemia 15.9% and hyperchloremia was seen in 26.0% severe patients. The distribution of sodium and potassium was significantly different ($p < 0.001$ and 0.001 respectively).

Sensitivity And Specificity Of Biochemical Markers For Covid-19 Severity

The ROC analysis of biochemical parameters was done to determine the sensitivity and specificity of these parameters to predict Covid-19 severity. Among liver function tests, an area under curve 0.79 for ALT suggest a good discrimination of severe and non-severe cases 60.2% sensitivity and 13.6% specificity Figure No 1. The total bilirubin levels on other hand found to be a bit poor severity predictor. Likewise, urea and creatinine provide 60.5% & 44.5% sensitivity, 11.1% and 12.3% specificity for Covid-19 severity respectively Figure No 1.



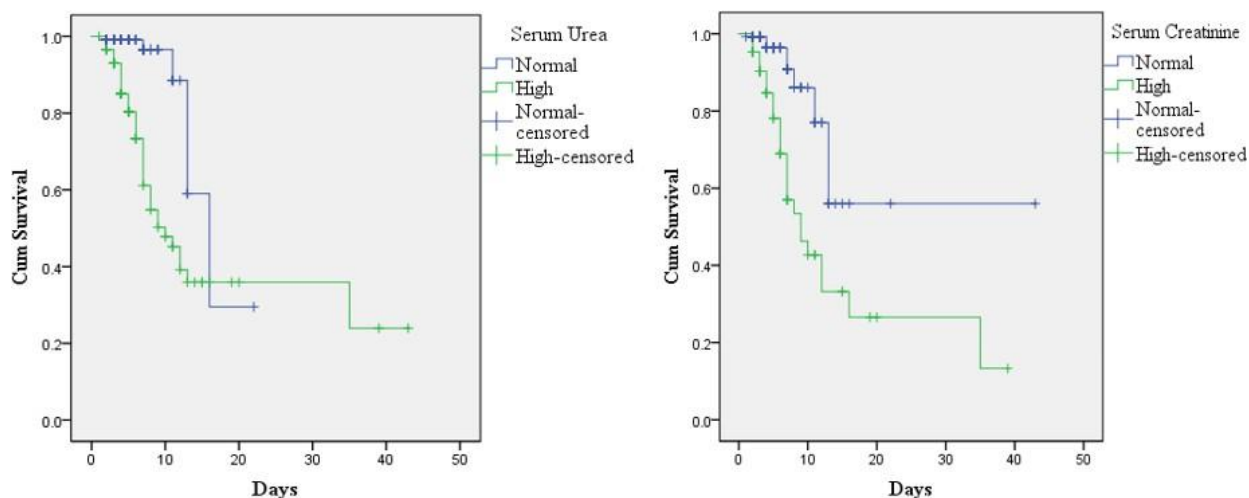
Parameter	AUC	Cut off	Sensitivity	1-Specificity	P-value
ALT	0.79	54.5	60.2%	13.6%	<0.001
T. Bil	0.61	1.1	-	-	0.007
Urea	0.834	61.5	60.5%	11.1%	<0.001
Creatinine	0.705	1.45	44.5%	12.3%	<0.001

Figure 1: Sensitivity and specificity (ROC analysis) of liver and Renal function parameters for Covid-19 severity.

Survival analysis of patients with de-ranged renal function tests and electrolytes

The Kaplan Meier survival analysis of patients with de-ranged biochemical patients was done to estimate the median survival time within hospital. Figure No 2 represents the survival curves of patients with deranged urea and creatinine. The median survival time of patients with high urea levels

was 10 days as compared to normal and the median survival time with high creatinine was 9 days as compared to normal. The survival curves of both parameters are statistically different.

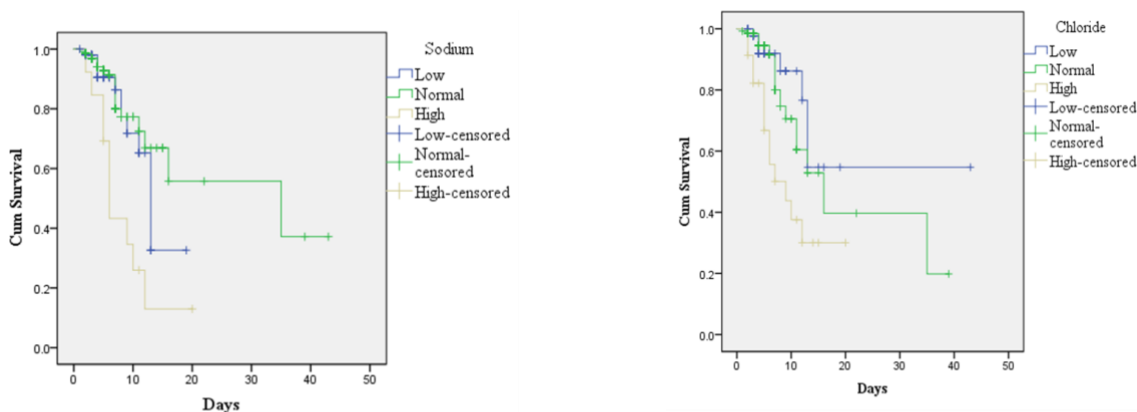


Urea	Estimate	Std. Error	95% Confidence Interval		P-value
Normal	16.000	2.308	11.477	20.523	<0.001
High	10.000	1.580	6.903	13.097	

Creatinine	Estimate	Std. Error	95% Confidence Interval		P-value
Normal	22.4	2.62	19.4	33.4	<0.001
High	9.000	1.765	5.541	12.459	

Figure 2: Survival analysis of patients with high levels of serum urea and creatinine by Kaplan Meier survival analysis the both parameters’ curves are statistically different from their normal and high levels (Log-Rank test) with P-values (<0.001)

Figure No 3 represents the survival analysis of patients with deranged sodium and chloride. Patients with low sodium levels median survival time was of 13 days and with high sodium levels was 6 days. Meanwhile with high levels of chloride the median survival time was 9 days. The survival curves of both parameters were statistically different.



Sodium	Estimate	Std. Error	95% C .I.		P-Value
Low	13.000	0.864	11.306	14.694	<0.001
Normal	35.000	13.421	8.694	61.306	
High	6.000	0.551	4.921	7.079	

Chloride	Estimate	Std. Error	95% C .I.		P-Value
Normal	16.000	3.345	9.444	22.556	<0.001
High	9.000	2.936	3.245	14.755	

Figure 3: Kaplan Meier survival analysis curve for Sodium and Chloride, both parameter’s curves are statistically significant (p<0.001)

Log-Rank test Lastly, binary logistic regression model was on biochemical parameters and the odd ratio for urea (OR=6.407 C. I 2.188-18.763, p<0.001) and creatinine (OR=2.941 C. I 1.134-7.628,

p=0.027) suggest them as independent mortality predictors in severe Covid-19 patients. Among Electrolytes, serum chloride is an independent mortality predictor with (OR=2.536 C. I 1.189-5.405, p=0.016).

Association of hematological parameters with Covid-19 severity

Among hematological markers, TLC was raised in 72.2% of severe patients, high neutrophil count was seen in 81.5% of severe patients, lymphopenia was observed in 33.6% of severe patients and low platelet count was seen in 18.4% of severe patients. The distribution of these parameters expect lymphocytes count is statistically different with respect to severe and non-severe and among deceased and survivor see Table No 3.

Coagulation markers, PT and APTT were prolonged in 84.8% and 68.0% of severe patients respectively and their distribution among severe and non-severe and in expired patients was statistically different see Table No 3.

Parameters	Severe				Non-Severe				P value	Expired				P value
	Low	Normal	High	Total	Low	Normal	High	Total		Low	Normal	High	Total	
TLC	0 (0.0%)	33 (27.7%)	86 (72.20%)	119	3 (3.7%)	56 (69.1%)	22 (27.1%)	81	**<0.001	NIL	9 (21.4%)	33 (78.5%)	42	**<0.001
Platelets	22 (18.4%)	85 (71.4%)	12 (10.0%)		5 (6.17%)	65 (80.2%)	11 (13.5%)		*0.028	11 (26.1%)	28 (66.6%)	3(7.14%)		*0.013
Neutrophil	0 (0.0%)	22 (18.4%)	97 (81.5%)		1 (1.2%)	56 (69.1%)	24 (29.6%)		**<0.001	NIL	4 (9.52%)	38(90.4%)		**<0.001
Lymph	40 (33.6%)	73 (61.3%)	6 (5.0%)		17 (20.9%)	62 (76.5%)	2 (2.4%)		0.315	20 (47.6%)	20 (47.6%)	2 (4.76%)		0.139
PT	NIL	18 (15.2%)	101 (84.8%)		NIL	44 (54.3%)	37 (45.6%)		**<0.001	NIL	3 (7.14%)	39(92.8%)		**<0.001
APTT	NIL	38 (31.9%)	81 (68.0%)		NIL	56 (69.1%)	25 (30.8%)		**<0.001	NIL	6 (14.2%)	36(85.7%)		**<0.002

Table 3: The distribution of hematological and coagulation markers in Covid-19 patients

Association of Neutrophil to lymphocyte ratio with Covid-19

Among non-severe patients, none of the patient were has NLR >18, and only 7.40% (n=6) patients have moderate stress, 28.3% (n=23) patients have NLR which indicate mild stress and 37.0% (n=30) patients have NLR between 4-5 and lastly 27.1% (n=22) have normal NLR. The distribution of NLR was statistically different (Man-Whitney U test) with P-value (<0.001).

Among severe Covid-19 patients, out of 119 patients 11.7% (n=14) patients have NLR >18 which indicate severe inflammatory stress, 34.4% (n=41) patients have moderate inflammatory stress having NLR within 9-18, 27.7% (n=33) patients have NLR within 6-9 which indicate mild stress and 19.3% (n=23) have NLR within 4-5 which is considered as grey zone Table 4. The distribution of NLR was statistically different (Man-Whitney U test) with P-value (<0.001).

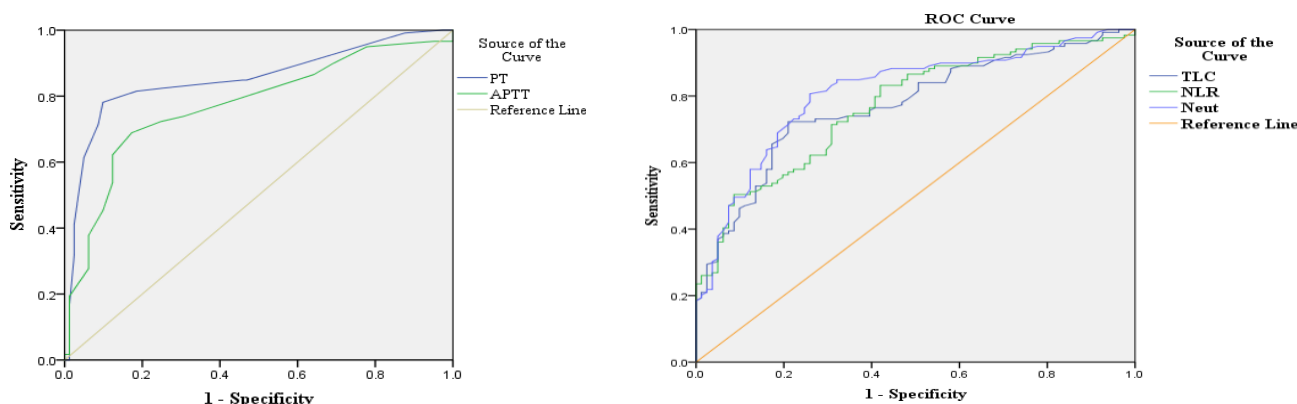
The neutrophil to lymphocyte ratio was also significantly different among patients who expired as compared to those of who discharged from hospital. Out of 42 total mortalities 16.5% (n=7) patients had severe inflammatory stress with having NLR >18, 42.8% (n=18) patients had moderate inflammatory stress with having NLR in between 9-18 and 30.9% (n=13) patients had mild stress with having NLR in between 6-9. The difference between two groups was statistically significant with p-value (p=<0.001) Table 4.

Parameter	Severity						Outcome		
	Range	N	Percent	Non-Severe	Severe	P-Value	Discharged	Expired	P-Value
Low	<1	1	0.0%	0 (0.0%)	1 (0.84%)	**<0.001	1 (0.63%)	0 (0.0%)	**<0.001
Normal	1-3	28	14.0%	22 (27.1%)	6 (5.04%)		28 (17.7%)	0 (0.0%)	
Grey Zone	4-5	53	26.5%	30 (37.0%)	23 (19.3%)		49 (31.0%)	4 (9.5%)	
Mild stress	6-9	56	28.0%	23 (28.3%)	33 (27.7%)		43 (27.2%)	13 (30.9%)	
Moderate stress	9-18	47	23.5%	6 (7.40%)	41(34.4%)		29 (18.3%)	18 (42.8%)	
Severe Stress	>18	14	7.0%	0 (0.0%)	14 (11.7%)		7 (4.4%)	7 (16.5%)	
Total		200	100.0	81	119		158	42	

Table 4: The distribution of neutrophil to lymphocytes ratio in severe, non-severe and expired and discharged Covid-19 patients

Sensitivity and specificity of hematological and coagulation parameters for Covid-19 severity

The details of sensitivity, specificity and cut values with their p-values for PT, APTT, TLC, neutrophil count and for neutrophil to lymphocytes ratio are given in Figure No 4. All the mentioned parameters can discriminate severe patients from non-severe with good sensitivity and specificity.



Parameters	Area	Cut off	Sensitivity	1- specificity	P-value
PT	0.853	18.5	61.3%	4.9%	**<0.001
APTT	0.774	39.5	62.2%	12.3%	**<0.001
TLC	0.772	12.8	52.9%	13.6%	**<0.001
Neut	0.812	9.1	62.2%	16.0%	**<0.001
NLR	0.770	8.15	53.8%	18.5%	**<0.001

Figure 4: ROC analysis of hematological and coagulation profiles.

Survival analysis of patients with de-ranged NLR

The Figure No 5 represent the median survival time of patients with de-ranged neutrophil to lymphocytes ratio. The median survival time for patients with NLR value within grey zone (4-5) was about 14 days, and the median survival time for patients with mild inflammatory stress was around 13 days whereas, patients with moderate inflammatory stress had a median survival time around 12 days. The most significant difference in median survival time was found in patients who had severe inflammatory stress with having NLR >18, the median survival time for these patients was 9 days. The survival curve of these patients has an immediate vertical steep and clear separation from other NLR categories which indicate a quicker event of death. The survival curve of NLR were different from each other (Log-Rank test) with statistically significant p-value ($p=0.002$)

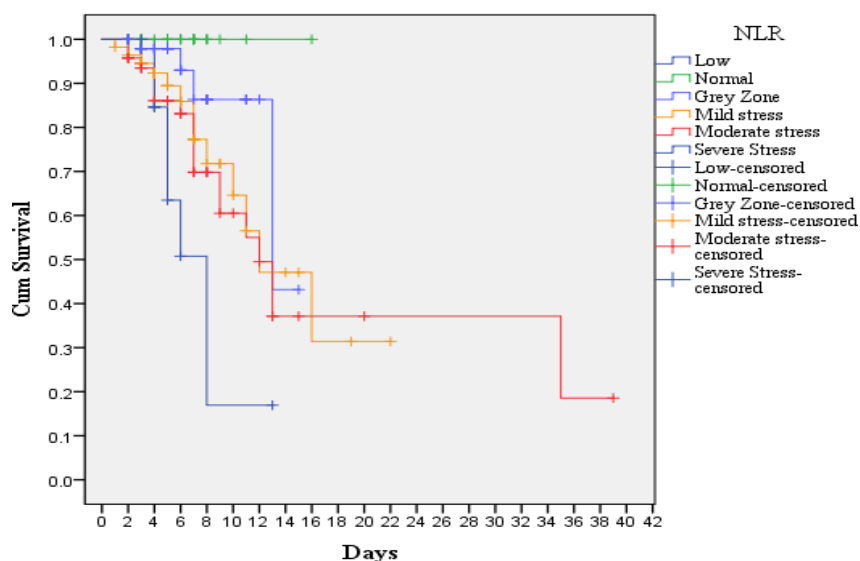


Figure 5: Kaplan Meier survival analysis of neutrophil to lymphocytes ratio in Covid-19 patients median survival time

Finally, the logistic binary regression analysis for hematological and coagulation markers was employed to determine the odds of mortality. Total leukocyte count, neutrophil count and neutrophil to lymphocytes ratio were statistically significant predictor for Covid-19 mortality among hematological markers. The odd ratio of (OR 4.148) for neutrophil count indicate it as independent mortality predictor with C.I (1.320-13.033) and p-value ($p=0.015$). The NLR was found to be also an independent mortality predictor in Covid-19 patients with odd ratio (OR 2.081 C. I at 95% 1.388-3.120) with p-value ($p<0.001$). For prothrombin time the odd ratio of 3.722 with C.I of (1.018-13.610) suggest that the odds of occurrence of death with increased PT are 3.722 times high with p-value (0.047) and For activated partial thromboplastin time the odd ratio of 4.873 with C.I (1.856-12.794) suggest that APTT is an independent predictor for mortality as well.

Discussion

The Covid-19 pandemic has caused drastic health and economic crises in Pakistan. This study demonstrates the relationship between demographics and various comorbidities with Covid-19 severity and mortality along with alteration in biochemical and hematological parameters. The data of age distribution revealed that there is an increased tendency towards hospital admissions with the advancement of age (13). The prevalence of different comorbidities, Diabetes Mellitus (DM), Hypertension (HTN), Ischemic Heart Disease (IHD), Chronic Obstructive Pulmonary Diseases (COPD), Chronic Kidney Disease (CKD), incidence of Acute Kidney Injury (AKI), asthma, pulmonary Tuberculosis (TB) was in line with previous literature (14). However, only diabetes mellitus, hypertension and ischemic heart disease were found to be significantly related with severe Covid-19 patients in this study (15). The in-hospital mortality incidence of 21% in this study is similar with previous studies (16). Among biochemical parameters, high ALT, total bilirubin levels were profound among severe patients (17). Increased urea and creatinine found to be independent mortality predictor within hospital setting (18). The hyponatremia was associated with severe Covid-19 disease and hypokalemia was not found significantly different among severe and non-severe patients however, the distribution of chloride was associated with Covid-19 mortality (19). Among hematological parameters high total leukocytes count, lymphopenia, neutrophilia and high neutrophil to lymphocyte ratio was profound among severe Covid-19 patients, having said that, TLC, neutrophil count and NLR were independent predictor of mortality in this study (20). Lastly, among coagulation markers PT and APTT were significantly high and found to be independent mortality predictor in hospitalized Covid-19 patients (21).

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