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RESEARCH ARTICLE

CLINICAL CHARACTERISTICS, LABORATORY ABNORMALITIES AND OUTCOME OF COVID-19 POSITIVE PATIENTS ADMITTED IN TERTIARY CARE HOSPITAL OF KARACHI.

Muhammad Farooq[1], Arshad ali[2], Furquana Niaz[3], Nadia Shams[4], Nasira Sohail[5], Urooj Tabassum[6], Nayyerul Islam[7] and Waquar Ahmed[8]

1. Associate Consultant, Associate Professor Internal Medicine King Abdullah Bin Abdul Aziz University Hospital, Princess NouraBint Abdurrahman University, Riyadh, KSA.
2. Associate Professor at Medicine Department at Karachi Institute of Medical Sceinces, Malir Cant. Karachi.
3. Associate Professor and Head of Dermatology Department at Karachi institute of Medical sceinces, Malir Cant. Karachi.
4. Professor & HOD Medicine at Rawal Institute of Health Sciences, Islamabad.
5. Assistant Professor of Medicine Department at Liyari General Hospital,Karachi
6. Assistant Professor of Psychiatry, Dow international Medical College,Dow University of Health Sciences,Karachi.
7. Professor, Associate Dean of Faculty & HOD Medicine, Karachi Institute of Medical Sceinces, Karachi.
8. Consultant Peadiatrician at WWL NHS Trust, UK.

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Abstract

Background and Objective:COVID-19 is a corona virus disease infecting people worldwide. There are few local small-scale studies addressing this. We planned a study with good sample size to reveal clinical features and laboratory abnormalities in relation to ICU admission and mortality.

Methods and Materials: This observational study was conducted at Dept. of Medicine Liyari General Hospital Karachi after ethical approval. The indoorconfirmed COVID-19 (PCR positive) patients (age>18 years) were included. Pregnant/lactating women, outdoor cases were excluded. Their demographic data, symptoms and signs,co morbidities, laboratory findings (blood complete picture, renal/liver function tests, inflammatory markers (i.e., CRP, ESR, ferritin, LDH, D dimers, troponins), area and duration of admission, disease severity, outcome as death or recovery were documented. Data was collected manually from record of the patients admitted from 15th March till 30th September 2020. The data was analyzed by SPSS software. Chi-square test applied with significant $p<0.05$.

Results: Amongst879 patients 773(87.9%) were admitted in isolation wards whereas 106(12.1%) admitted in ICU. Mortality was 3.9% overall and average length of stay was 11 days. The mean age was 51.8+18.4 years. Most cases were male (65%) and > 50 yearsage (58.9%).Frequent co morbidities were diabetes(26.1%), dyslipidemia (23%), hypertension (19.9%) and ischemic heart disease (17.3%). Fever wasmost common symptom. Tachycardia, hypotension, anemia and lymphocytopenia wereassociated with ICU admission and mortality.Inflammatory markers were elevated in most of the cases but

Corresponding Author:-Muhammad Farooq
Address:-Associate Consultant And Associate Professor Internal Medicine king Abdullah Bin Abdul Aziz University Hospital, Princess NouraBint Abdurrahman University, Riyadh, KSA.

only LDH, ferritin and D-dimers were statistically associated with ICU admission and mortality.

Conclusion: This study concludes that COVID-19 positive patients with age above fifty, tachycardia, hypotension; elevated LDH, Ferritin, D dimers; anemia and lymphocytopenia were associated with mortality and ICU admission.

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Introduction: -

The corona virus is new pathogen identified in WuhanChina in December 2019. This was named as SARS COV II (severe respiratory distress syndrome Corona virus 2) and then named as COVID -19 (corona virus disease 2019) by World Health Organization. [1-3]WHO declared COVID-19 as pandemic on 11 March 2020 in view of its global spread [4]. According to the recent WHO COVID-19 situation reports, a total of 113,076,707 individuals have been infected, with 2,512,172 confirmed deaths [5]. Pakistan has 579,973 cases (258,004 in Sindh, 171,349 in Punjab, 72,162 in Khyber Pakhtunkhwa,19,045 in Baluchistan, 4,956 in Gilgit-Baltistan and10, 198 in Azad Kashmir) with 12,860 deaths as of February 28, 2021 [6]. The rampant nature of SARS-CoV-2 is due to its high infectivity. The virus can be transmitted from human to human through physical contact and respiratory droplets produced by coughing, or sneezing [7].

The main clinical manifestations of SAR-CoV-2 range from mild asymptomatic disease to life threatening complications. Initially, the patient presents with cough, fever, dyspnea, and fatigue. Other less common complaints may include diarrhea, headache, and the production of sputum. The disease can progress to cause pneumonia, leucopenia, and lymphocytopenia. [8] Laboratory findings detected in the majority of COVID-19 disease sufferers are lymphocytopenia (82.3%), thrombocytopenia (36.2%), leucopenia (33.7%), majority of patients reported high levels of C-reactive protein (CRP), less frequent were high levels of alanine transaminase (ALT), aspartate aminotransferase (AST), creatinine kinase (CK) and D-dimer [9].

Pakistan as poor resource country in health care responded in this pandemic quite carefully by putting the standards for preventive methods, highlighting in media, implementing restrictions on social gatherings and making social distancing mandatory, implementing lockdown in areas of spread of infection and practicing quarantine for infected cases. The objective of this study was to find out commonest clinical presentations, predictors of mortality and requirement of critical care in Covid affected cases. These may be helpful for early detection, quarantine of infected patients and to organize management plan and arrange resources for moderate to severe covid-19 infection cases. The ultimate aim is to avoid complications and improve mortality.

Methodology: -

Study design and setting:

This study was conducted as a single centered, observational study. The study conducted on Covid-19 positive patients admitted in Liyari General Hospital Karachiduring period of 15th March till 30th September, 2020 afer ethical approval. The patients < 18 years, Pregnant/ lactating females were excluded from the study. Consent was obtained from all cases upon admission.

Data collection:

A predesigned and unified data collection form was designed to collect pre-specified data variables from ward and ICU patient's medical records by trained physicians. All the data collected were used for the benefits of the present study only. Patient demographics, co morbidities, clinical signs or symptoms and laboratory results were all obtained through the data collection form. The study population was divided into two age groups: Group 1:18–<50 years Group 2: >50 years.

Operational Definitions:

The COVID-19 was considered positive via nasopharyngeal swab for PCR. The diagnostic kit used exploits the principle of real-time fluorescence (RT-PCR), USA-WA1/2020 stock concentration 2.8E+05 TCID50/mL, with a lower detection limit of 0.003 TCID50/mL [10].

1. **Disease severity:**The confirmed cases were clinically classified as mild, moderate, severe and critical, according to the National Institute of Health, Pakistan guidelines and are defined as below. [11].
- **Milddisease**was defined as only presence of symptoms of fever, cough, shortness of breath, headache, malaise, taste change, loss of smell without requiring oxygen and hemodynamic ally stable.
- **Moderate** was defined as high grade fever with some hypoxia that may require minimal oxygen inhalation.
- **Severe** was defined as shortness of breath with hypoxia with finding of pneumonia but hemodynamic ally stable.
- **Critical** was defined as severe respiratory distress (can't speak in sentences), severe hypoxia, respiratory rate more than 30 breaths/min, central cyanosis, confusion, agitation, signs of shock, or signs of heart failure ore urine output less than 0.5ml/kg/hour or systolic blood pressure less than 90mmHg.

2. **The hospital length of stay** was defined as the period between the date of admission to the date of discharge or the date of transfer to another hospital or the date of expiry.
3. **Recovered case:**Patients who were discharge from the hospital were considered recovered and patient staying in the hospital for other co morbidities but remain asymptomatic for >72 hours were considered as recovered.

Statistical analysis:
The data was analyzed using SPSS (V.24.0). A value of $p < 0.05$ was considered statistically significant. Distribution of the continuous variables was carried out by student t test. Chi-square test was employed to detect the relationship between the categorical variables.We calculated length of stay from the date of admission to date of discharge/death. Then we analyzed the length of stay according to admission in ward or ICU.

Results: -

Out of total 879 patients 575(65.4%) were males while 304(34.6%) were females with ratio of 1.9:1. There was no difference between ward or ICU admission in terms of mortality or recovery of patients regarding gender. The mean age of our patients was 51.82 years and the range was from 18 years to 83 years. Most of the patients were above the age of 50 years (58.9% vs. 41.1%). Patients more than 50 years were more prone to be admitted to ICU **(p=0.041)** and had a higher mortality as compared to age less than 50 years **(p=0.049)**. Most of the patients (84%) had mild to moderate infection and were admitted mostly in wards with no obvious complications observed and no mortality was found in this group. Patients with severe and critical illness (16%) were admitted in ICU and almost one fourth mortality (25%) was observed.

The most common co morbidity was diabetes (26.1%) and it was observed that patients with diabetes had significantly increase chance of admission in ICU **(p=0.032)** and mortality **(p=0.045).** The second common co morbidity was dyslipidemia (23%) but there was no association of admission in ICU or mortality with dyslipidemia**(p>0.05).** The other important co morbidity was hypertension 19.9% which was also associated with ICU admission **(p=0.042)** and mortality **(p=0.048).** The other co morbidities were less common and not associated with ICU admission or mortality except chronic kidney disease which has statistical significance for ICU admission **(p=0.045)** and mortality **(p=0.042).**

Fever was most frequent symptom but it was not related with ICU admission **(p=0123)** or mortality **(p=0.089).**The other frequent symptoms were dry cough (52.1%), dyspnea (43%), chest pain (16%), fatigue, and gastro intestinal symptoms. There was no association of symptoms with ICU admission or mortality.

Tachycardia was seen in 264(41.5%) patients and it was related significantly with ICU admission and mortality **(p=0.04).** Decreased oxygen saturation (<94%) was seen in 417(47.5%) patients and it was more in ICU cases and cases that expired**(p=0.049**and **0.021**respectively). high grade temperature (>102^{o}F) was seen in 264(28%) patients with no statistically significant difference in ICU and ward admission or mortality and recovery. Tachypnea (R/R>24) was seen in 233(26.3%) patients. There was no statistically significant difference in ward or ICU admission or mortality to recovery regarding tachypnea. SBP <90mmHg was seen in few patients (9.5%) as DBP <60mmHg in 9% patients. Both were related with more ICU admission and mortality. (Table)

Severe anemia (Hb<5g/dl) was seen in 117(13.3%) patients that was significantly more in ICU patients**(p=0.042)** and was related to mortality **(p=0.045).**Leucopaenia observed in 219(24.9%) patients but it wasn't significant statistically for ICU admission or mortality**(p>0.05).**Lymphocytopaenia was seen in 261(29.7%) patients and had statistical significance for ICU admission and mortality **(p=0.034**and**0.041** respectively). Whereas thrombocytopenia

more frequently found (32.3%) but not having any statistical significance regarding ICU admission or mortality **(p=0.06**and **0.213** respectively).

Other laboratory abnormalities revealed that most of the inflammatory markers were elevated but didn't have statistical significance regarding ICU admission and mortality except LDH, ferritin and Ddimer which were markedly elevated in ICU and expired patients. High blood sugar was also reported significantly higher in ICU patients related withmortality.

Variables	Total n=879	Ward n=773	ICU n=106	P-value	Death n= 35	Recovered n=844	P-value
Age (years)							
• < 50 Years	361(41.1%)	329(42.5%)	32(30.1%)	0.082	11(31.4%)	350(41.4%)	0.091
• > 50 Years	518(58.9%)	454(58.7%)	64(69.8%)	0.04*	24(68.5%)	494(58.5%)	0.049*
Gender							
• Male	575(65.4%)	501(64.8%)	74(69.8%)	0.098	26(74.2%)	549(65%)	0.061
• Female	304(34.6%)	272(35.1%)	32(30.1%)	0.124	9(25.7%)	295(34.9%)	0.089
Symptoms							
• Fever	729(83%)	640(82.7%)	89(83.9%)	0.123	32(91.4%)	697(82.5%)	0.089
• Dry Cough	457(52%)	403(52.1%)	54(50.9%)	0.231	21(60%)	436(51.6%)	0.098
• Dyspnea	378(43%)	332(42.9%)	46(43.3%)	0.089	15(42.8%)	363(43%)	0.089
• Productive Cough	158(18%)	140(18.1%)	19(17.9%)	0.094	7(20%)	151(17.8%)	0.097
• Diarrhea	149(17%)	139(17.9%)	10(10.6%)	0.096	6(17.1%)	143(16.9%)	1.243
• Chest Pain	141(16%)	137(17.7%)	4(3.7%)	0.06	4(11.4%)	137(16.2%)	0.071
• Sore Throat	141(16%)	125(16.1%)	16(15.1%)	0.145	6(17.14%)	135(15.9%)	0.213
• Fatigue	141(16%)	126(16.3%)	15(14.1%)	0.087	8(22.8%)	133(15.7%)	0.067
• Rhinitis	132(15%)	127(16.4%)	14(13.2%)	0.21	7(20%)	134((15.8%)	0.071
• Myalgia	123(14%)	107(13.8%)	16(15.1%)	0.245	6(17.1%)	117(13.8%)	0.065
• Loss of Taste	70(8%)	61(7.8%)	9(8.4%)	0.097	3(8.5%)	67(7.9%)	0.074
• Loss of Smell	79(9%)	69(8.9%)	10(9.4%)	0.085	3(8.5%)	76(9%)	0.067
• Lethargy	97(11%)	85(10.9%)	12(11.3%)	0.067	4(11.4%)	93(11%)	0.089
• Headache	70(8%)	60(7.7%)	10(9.4%)	0.145	4(11.4%)	66(7.8%)	0.094
• Vomiting/Diarrhea	62(7%)	54(6.9%)	8(7.5%)	0.081	2(5.7%)	60(7.1%)	0.213
• Abdominal Pain	53(6%)	45(5.8%)	8(7.5%)	0.074	3(8.5%)	50(5.9%)	0.156
Vital Signs							
• Temp >102^{o}F	264(28%)	234(30.2%)	30(28.3%)	0.063	9(25.7%)	255(30.2%)	0.087
• R/R** >24	233(26.5%)	205(26.5%)	28(26.4%)	0.32*	10(28.5)	223(26.4%)	0.091
• Pulse>100	365(41.5%)	294(38.03)	71(66.9%)	0.04*	22(62.8%)	343(40.6%)	0.04*
• O2 Sats<94%	417(47.5%)	348(45%)	69(65.1%)	0.05*	23(65.7%)	394(46.6%)	0.021*
• SBP***<90mmHg	84(9.5%)	37(4.7%)	47(44.3%)	0.01*	13(37.1%)	71(8.4%)	0.01*
• DBP****<60mmHg	79(9%)	38(4.9%)	41(38.6%)	0.01*	14(40%)	65(7.7%)	0.012*
Length of stay(days)	11.2	7.8	15.3	0.04*	12	7.1	0.032*

(*Significant p-value <0.05, test of significance Chi-square test)
respiratory rate,*systolic blood pressure,****diastolic blood pressure

Table 1:- Comparison of demographic data, clinical features and mortality in ward and ICU patients **(n=879).**

Co morbidities	Total n=879	Ward n=773	ICU n=106	P-value	Death n= 35	Recovered n=844	P-value
• Diabetic	229(26.1%)	158(20%)	71(66%)	0.032*	26(74%)	203(24%)	0.045*
• Hypertensive	175(19.9%)	130(17%)	45(42%)	0.042*	21(60%)	154(18%)	0.048*
• Dyslipidemic	202(23%)	171(22%)	31(29%)	0.134	9(26%)	164(18%)	0.281
• Smoker	97(11%)	76(9%)	21(19%)	0.106	2(6%)	95(11%)	0.314
• Obesity	160(18.2%)	134(17%)	26(24%)	0.31	7(20%)	153(18%)	0.241
• IHD**	152(17.3%)	141(18%)	11(10%)	0.132	9(25.7%)	143(16.9%)	0.081

• CLD***	50(5.7)	38(5%)	12(1%)	0.092	4(11.4%)	46(5.4%)	0.156
• CKD****	60(6.8%)	47(6%)	13(12%)	0.045*	16(45.7%)	44(5.2%)	0.042
• CVA*****	28(3.2%)	19(3%)	9(8%)	0.158	3(8.5%)	25(2.9%)	0.256
COVID Severity							
• Mild	373(42.4%)	373(48)	0(0%)	0.01*	0(0%)	373(44.1%)	0.01*
• Moderate	366(41.6%)	365(47.5%	1(1%)	0.02*	0(0%)	366(43.3%)	0.01*
• Severe	105(12%)	35(4.5%)	70(66%)	0.043*	4(11.4%)	101(11.9%)	0.091*
• Critical	35(4%)	0(0%)	35(33%)	0.015*	31(88.5%)	4(0.4%)	0.021*

(*Significant p-value<0.05, test of significance Chi-square test)
ischemic heart disease,*chronic liver disease,****chronic kidney disease,*****cerebrovascular accident)

Table 2:- Comparison of co morbidities in ward and ICU patients **(n=879).**

Laboratory finding	**Total n=879**	**Ward n=773**	**ICU n=106**	**P value**	**Death n= 35**	**Recovered n=844**	**P-value**
Hb**<5	117(13.3)	72(1%)	45(43%)	0.042*	8(22.8%)	109(12.9%)	0.045*
Leucopenia	219(24.9)	201(26%)	18(17%)	0.894	5(14.2%)	214(25.3%)	0.123
Lymphopenia	261(29.7)	165(21%)	96(90.9%)	0.034*	9(25.7%)	252(29.8%)	0.041*
Thrombocytopenia	284(32.3)	262(33%)	22(21.2%)	0.06	1131.4%)	251(29.7%)	0.213
CRP***>10	668(76)	567(73%)	101(96%)	0.071	32(91.4%)	636(75.3%)	0.091
ESR>20mm/hr	606(69)	503(65%)	103(98%)	0.061	30(85.7%)	576(68.2%)	0.081
LDH>250	374(42.6)	270(34%)	104(99%)	0.045	26(74.2%)	348(41.2%)	0.03
Ferritin>250	318(36.2)	223(28.8)	95(89.9%)	0.021*	31(88.5%)	287(34%)	0.032
D DIMER>0.5	274(31.2)	171(22%)	103(98%)	0.012*	21(60%)	253(29.9%)	0.042*
Troponin>34pg/ml	216(24.6)	163(21%)	53(50%)	0.061	18(51.4%)	198(23.4%)	0.082
CK>250	206(23.5)	144(18%)	62(59%)	0.12	21(60%)	185(21.9%)	0.214
ALT>45	220(25)	149(19%)	71(67.6%)	0.091	19(54.2%)	201(23.8%)	0.87
AST>45	237(27)	199(26%)	38(36%)	0.145	21(60%)	178(21%)	0.213
Creatinine>1.5	207(23.6)	166(21%)	41(39.3%)	0.213	25(71.4%)	182(21.5%)	0.21
Urea>50	147(16.7)	93(12%)	54(51.5%)	0.082	23(65.7%)	124(14.6%)	0.091
RBS	220(25)	155(20%)	65(61.5%)	0.045*	21(60%)	199(23.6)	0.041*

(*Significant p-value <0.05, **hemoglobin, ***C-reactive protein)
Table 3:- Comparison of co morbidities and mortality in ward and ICU patients **(n=879).**

Discussion:-

Liyari General Hospital Karachi is a tertiary care hospital dealing with Covid cases as well. People from all areas of city of Karachi and rural areas of Sindh get medical care in this hospital. It is a large hospital with around 600 bed capacity. During the pandemic, symptomatic patients were admitted for observation and care but asymptomatic cases were not admitted to our hospital. Such patients were either going to special quarantine centers or home isolation.

In our study male patients were almost double than female patients (Ratio1.9:1). This is synchronizing with findings of multiple studies[1-3] while contrasting with the results of a study by Liu K in which females were more than males [3], although there was no significant difference in gender statistically regarding admission to ICU or mortality.

Almost sixty percent (58.9%)were above age of 50 years and mean age was almost 52+18.4 years coinciding with findings of various studies, indicating that this novel disease commonly infects middle-aged and older population and. Increasing age was related with ICU admission and mortality [3-4,8-9,12-14].

Most of the patients had mild to moderate disease with no mortality. Only sixteen percent of our patients had severe to critical disease. Overall mortality was almost four percent (3.9%) which was related the severe and especially critical disease. Out of all the hospitalized patients, 12% required ICU care. COVID-19 case fatality rate was 3.9% among the hospitalized, and 33% among those admitted to the ICU. Patient's age, co morbid conditions and certain laboratory abnormalities were associated with poor in-hospital outcomes in COVID-19 patients as mentioned in

other study [15].The mortality among our critically ill cases (33%) was less than to the case series from Seattle, USA (50%), but similar to the study from New York, USA (39%).[15,16,17]

Out of all co morbidities, 26.1% had diabetes, 19.9% had hypertension, 23% dyslipidemiaand 17.3% had ischemic heart disease. Diabetes and hypertension were related with ICU admission and mortality which are correlating with findings of many studies [3, 9, 12-13]. High percentage (83%) of fever reported in our study, which concedes with early studies from China (90%) during their peak of the epidemic, but some studies revealed low percentage like 31% in New York, USA and 45% in Europe [18]. Other Frequent symptoms were dry cough, dyspnea and chest pain but gastrointestinal symptoms were only seen in thirteen percent of patients which was same as in other local study [19]. Loss of taste was seen only in 8 percent and loss of smell in 9 percent of patients. These manifestations synchronize with manifestations reported in several studies.[7,12-14]

Tachycardia was seen in 41.5% patients and it was related significantly with ICU admission and mortality. Decreased oxygen saturation (<94%) was seen in approx. half (i.e., 47.5%) of patients and it was more in ICU and expired patients. These finding were same as seen in a study from Saudi Arabia that revealed pulse rate on admission was higher (110 Vs. 103) and oxygen saturation was lower (82% Vs. 88 %). [20]

High grade temperature (>102^{o}F) was seen in 28% patients with no statistically significant difference in ICU and ward admission or mortality and recovery. Tachypnea (R/R >24) was seen in 26.3% patients. There was no statistically significant difference in ward or ICU admission or mortality to recovery regarding tachypnea. SBP <90mmHg was seen in few patients (9.5%) as DBP in 9% patients. Both were related with ICU admission and mortality. The reason being that these patients were admitted directly in intensive care due to shock, hence the mortality was higher with low blood pressure as seen in a local study as well.[19]
Severe anemia (Hb<5g/dl) was seen in 13.3% patients which was statistically significant in ICU patient compared to ward patients (p=0.042) and related to mortality (p=0.045). Which is coinciding with other studies (19). Leucopenia was observed in 219 (24.9%) patients but it was not significant statistically for ICU admission or mortality. This is in contrast to a local study in which leukocytosis was observed and related with ICU admission 20(local). Lymphopenia was seen in 261 (29.7%) patients and had statistical significance for ICU admission and mortality (p=0.034, 0.041 respectively) which is coinciding with finding of same local study with small sample size. Thrombocytopenia more frequently found (32.3%) but not having any statistical significance regarding ICU admission or mortality (p=0.06, 0.213 respectively). Which is similar to other study [21]but contrasting to the local study (local) whereas increase platelets count was seen in mild to moderate disease in one study [22].

The most of the inflammatory markers were elevated but not had statistical significance regarding ICU admission and mortality except LDH, ferritin and D-Dimers which were markedly elevated in ICU and expired patients. Blood sugar was reported significantly higher in ICU and expired patients which is also Coinciding with results of numerous studies [12-14]. C-reactive protein, which is a protein produced by the liver, was found to be a relatively good predictor for the development of pneumonia and has recently been found to be an important marker to anticipate the possibility of deterioration of COVID-19 patients, with an optimal threshold value of 26.9 mg/L (28, 23). This finding also reflected in our study. Hence, 76% of our patients had high CRP and it was more in ICU patients (96%) but it was not statistically significant predictor for ICU admission or mortality same as in another local study [20]. Other markers which possibly predict severe COVID -19 infections like high Ddimer, high ferritin, and high blood sugar were also reported in our study which is also reported in previous studies [15-16, 23-26].

The average length of stay in our hospital was eleven days. It was 7 to 8 days for recovered and wards patients but patients requiring ICU care stayed up to 15 days as average. This finding also coincides with findings of a local study in which average stay in hospital was 8 daysand other studies [13-14].

There were a few limitations in our study, the one being a single center study and data is taken only for admitted cases. Because of retrospective analysis all laboratory parameters were not continuously monitored in the patients. Another limitation is that the radiological investigationsweren't included in the study.

In summary, despite the limitations of the study the sample size was quite good compared to other studies done in same city with small sample size. This study is describing clinical characteristics and outcome of hospitalized COVID-19 patients in a country with limited resources. Further studies are needed to include radiological investigations with comparison of clinical features of COVID-19 patients.This study invites the other investigator to

do more studies with prospective study design to find out proper relationship in ICU admission and mortality with clinical features.

Conclusions:-

This observational study on confirmed COVID-19 cases revealed that most of the patients were male and of age was above 50 years. The most of cases had mild to moderate disease and only some had severe or critical illness and admitted to ICU.ThelCU admission and mortality were related with increasing age, severe to critical illness, severe anemia, lymphocytopenia, high ferritin and D-dimer. The COVID case with tachycardia, low blood pressure and high D-dimer should be managed in ICU.

Authors' Contribution

Muhammad Farooq is the primary investigator.He conceived the idea and designed the study. He also checked the final data and wrote the manuscript for final publication. Arshad Ali was the research coordinator, maintaining the online data sheets and updated the data from time to time. He was also involved in extracting the data from files manually. Rest of the authors contributed to data collection, analysis, writeup and literature review.

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None.

Conflicts Of Interest:

There was no conflict of interest of any authors.

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