

Original Article

Clinical and Biochemical Profile of Patients with COVID - 19 Infection; A Multicenter-Retrospective Study from three Tertiary Care Hospitals of Lahore, Pakistan

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Abstract

Objectives: To assess the clinical and biochemical profile of patients with Covid – 19 infection in three major tertiary care hospitals of Lahore, Pakistan.

Methods: Retrospective observational study involving three tertiary care hospitals of Lahore. Fatima Memorial Hospital, Services Hospital and Jinnah Hospital, Lahore. Sample Size: Total 100 patients; Study duration: 2 months, 15th October to 15th December, 2020.

Results: A total of 100 patients hospitalized with Covid-19 infection were observed in this retrospective study. The commonest symptoms observed were fever, shortness of breath and cough with 80.4%, 63.0% and 57.6% percentages respectively. Diabetes was the most prevalent pre-existing condition with 29% men and 21% women known to have the disease. Although, many more male patients required oxygen n= 47 than female patients n = 26, the p-value wasn't significant (p-value = 1.000). Our observational study also demonstrated lymphopenia in both gender groups with median lymphocyte count being 14. The total neutrophil count was a median =77 with IQR = 22.0. The neutrophil-to-lymphocyte ratio was 5.85 (median). We observed higher levels of inflammatory markers in men as compared to women. Median CRP of 74 versus 27.28 in men and women respectively. Median serum ferritin of 635.93 in men compared to median of 361.00 in women. Both values correspond to increased disease severity in men. We observed a total d-dimer median of 1.13 (IQR 3.24) with no difference between our gender groups (p-value = 0.797). We observed patients Troponin I was recorded as median of 5.90 in male patients compared with median of 3.60 in female patients. Our cohort of patients demonstrated a median serum creatinine of 0.99 (IQR = 0.51).

Conclusion: Patients with multiple co-morbidities and having high Neutrophil to lymphocyte ratio, increased inflammatory markers and raised markers of organ dysfunction are at increased risk of developing severe disease with gender variation too as males are more prone to develop severe infection.

Keywords: Covid-19, SARS- CoV, Biochemical Profiles, Lahore

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Introduction

Human corona viruses were first described in 1960. Since then 6 subtypes have been identified. Of these, most notable have been Severe Acute Respiratory Syndrome (SARS) and Middle Eastern Respiratory Syndrome (MERS) in recent years. On 31st December

2019, World Health Organization (WHO) was formally notified regarding a cluster of cases of pneumonia being caused by a novel corona virus, identified as acute respiratory syndrome coronavirus-2, SARS-CoV-2.¹ Phylogenetic analysis suggested that SARS-CoV-2 was started via a zoonotic transmission from

animals, probably bats to humans.² The subsequent pandemic was however due to human to human transmission. The disease caused by SARS-CoV-2 is called Corona virus disease 19, COVID-19. In March 2020, WHO declared COVID-19 as a pandemic. Globally, as of February 2021, there have been over one hundred million confirmed cases of COVID-19, including over 2 million deaths, reported to WHO.³

Various studies showed evidence that SARS-CoV-2 primarily affects the respiratory system; however other organ systems may also be affected. SARS-CoV-2 attaches itself to the host ACE-2 receptors via its spike protein.⁴ ACE2 expression is high in lung, heart, ileum, kidney and bladder and also on innate lymphoid cells and endothelial cells.⁵ Host response to the virus also plays an essential role in how the disease progresses and whether the patient develops cytokine storm. Higher levels of cytokines such as IL-2, TNF-alpha, IL-10 were found in plasma of patients with severe COVID-19 disease. Another study showed evidence of hyper-functioning of both CD4 and CD8 T cells leading to severe disease.⁶ This may explain the heterogenous symptoms experienced by COVID-19 patients ranging from asymptomatic disease to severe ARDS.

Our study aims to describe the clinical and biochemical characteristics in patients admitted with COVID-19 disease in four different hospitals in Lahore. This will provide a better understanding of correlation between the demographic and biochemical profiling of patients with COVID-19 disease. It will also help us in diagnosis, disease monitoring and predicting disease severity based on clinical and biochemical markers.

Methods

Study Design And Settings: Retrospective observational study involving three tertiary care hospitals of Lahore. Total 100 patients (>16 years) were included who had mild to severe disease caused by COVID-19

Inclusion Criteria: All patients above 16 years, with COVID-19 infection proven by positive PCR test taken through a nasopharyngeal swab.

Exclusion Criteria: Negative Covid-19 PCR and patients under 16 years

Data Collection Procedure: All patients admitted in wards and intensive care unit in the participating centers were studied and data related to demographics, clinical, laboratory, radiological results, was collected using a structured Performa.

Data Analysis: Outcomes analyzed using SPSS 23.0. Frequency and percentages were calculated for the qualitative variables like gender, co-morbidities and symptoms. Quantitative variables of the study like

age, laboratory parameters were expressed as Mean \pm SD.

Ethical Considerations: Appropriate consent was taken from participants before data collection. Approval was also taken from the ethical review committee.

Results

A total of 100 patients hospitalized with Covid-19 infection were observed in this retrospective study. Patients with certain demographic characteristics were observed as more susceptible to Covid-19 infection such as older age group, patients with diabetes, hypertension and ischaemic heart disease.

Age:

The median age of patients was 58 and IQR of 20. The p-value = 0.910 suggests no difference with regards to age between our observed male and female groups. The median age in men being 59 with IQR 23, whilst in women median age was 57 with IQR of 19.

Presenting Symptoms

The commonest symptoms observed were fever, shortness of breath and cough with 80.4%, 63.0% and 57.6% percentages respectively. A higher number of male patients with Covid-19 infection presented with fever (mean = 45) versus female patients (mean= 29), shortness of breath (mean=41) versus female patients (mean = 17) and cough (mean = 35) versus female patients (mean=18). Other symptoms, such as diarrhoea, anosmia, sore-throat and chills were also observed only in male sex patients. However, despite this apparent inequality, no statistically significant difference was found between the two genders.

Co-morbidities:

Table 1: : Frequency of Presenting Symptoms in our COVID-19 Patients (Gender distribution too)

	Male. N (%)	Female N (%)	Total N (%)	p – value
Cough	35 (38.0%)	18(19.6%)	53(57.6%)	1.000
Fever	45(48.9%)	29(31.5%)	74(80.4%)	0.099
Shortness of breath	41 (44.6%)	17(18.5%)	58(63.0%)	0.177
Myalgia	5(5.4%)	3(3.3%)	8(8.7%)	1.000
Vomiting	0(0.0%)	2(2.2%)	2(2.2%)	0.118
Diarrhoea	1 (1.1%)	5 (5.4%)	6 (6.5%)	0.018
Anosmia	2 (2.2%)	0 (0.0)	2 (2.2%)	0.541
Sore throat	2 (2.2%)	0 (0.0%)	2 (2.2%)	0.541
Chills	2 (2.2%)	0 (0.0%)	2 (2.2%)	0.541

Diabetes was the most prevalent pre-existing condition with 29% men and 21% women known to have the disease. Hypertension, the second most frequent

condition was found in 27% male patients and 17% female patients, p value = 0.678. A total of 17 patients had history of cardiovascular disease, mainly ischaemic heart disease. Chronic kidney disease was found in 7% of men and 4% of women. Other background illnesses included obesity, asthma. The difference between both genders was not found to be statistically significant as p value was >0.005 for all co-morbid illnesses.

Table 2: Co-Morbidities in Male and Female Patients with Covid-19

Co-morbidities	Male	Female	Total	P-value
Diabetes	29 (29.0%)	21 (21.0%)	50 (50.0%)	0.298
Hypertension	27 (27.0%)	17 (17.0%)	44 (44.0%)	0.678
Cardiovascular Disease	14 (14.0%)	3 (3.0%)	17 (17.0%)	0.102
Chronic Kidney Disease	7 (7.0%)	4 (4.0%)	11 (11.0%)	1.000
Others	6 (6.0%)	3 (3.0%)	9 (9.0%)	1.000

Oxygen Requirement

Although, many more male patients required oxygen $n=47$ than female patients $n=26$, the p -value wasn't significant (p -value = 1.000). However, this finding corroborates with other studies where data suggests male sex is a variable that is associated with severe infection with COVID-19.⁷

Total Leukocyte Count and Differential

Multiple researches on the differential white cell count in COVID-19 patients have shown correlation between lymphopenia and severity of COVID-19 infection.⁸ Our observational study also demonstrated lymphopenia in both gender groups with median lymphocyte count being¹⁴. The total neutrophil count was a median=77 with IQR = 22.0. The neutrophil-to-lymphocyte ratio was 5.85 (median). The p -values for the total leukocyte count, neutrophil count, lymphocyte count and NLR were all >0.005 , indicating no differences between the two groups.

Inflammatory Markers

Non-specific markers of cellular injury have been used to assess disease severity in COVID-19. These include C-reactive protein, Serum Ferritin and lactate dehydrogenase (LDH). We observed higher levels of these inflammatory markers in men as compared to women. Median CRP of 74 versus 27.28 in men and women respectively. Median serum ferritin of 635.93 in men compared to median of 361.00 in women. Both values correspond to increased disease severity in men. Median serum LDH in male patients = 349.00, while median serum LDH in female patients = 321.00.

Elevated D-dimers have been associated with extensive thrombus formation mainly in the lung vasculature resulting in ventilation perfusion mis-match. Coagulopathy in COVID-19 patients is associated with increased mortality.⁹ We observed a total d-dimer median of 1.13 (IQR 3.24) with no difference between our gender groups (p -value = 0.797).

Markers of Organ Dysfunction

COVID-19 has been linked to systolic dysfunction and myocarditis.¹⁰ However in our observed patients Troponin I was recorded as median of 5.90 in male patients compared with median of 3.60 in female patients. Our cohort of patients demonstrated a median serum creatinine of 0.99 (IQR = 0.51). Also serum alanine aminotransferase levels (ALT) were noted as median of 43.00 in male patients versus 40.50 in female patients (p -value = 0.343).

Discussion

This is the unique study which was conducted in second largest city of Pakistan, Lahore that has taken into consideration about age, gender, obesity and multiple comorbidities along with hematological and biochemical parameters that have been strongly associated with adverse outcomes in this novel disease. Our study described the baseline characteristics, clinical features of 100 patients with Covid-19 infection. Total of 100 patients were observed in this retrospective study, all the patients were hospitalized

Table 3: Table.3. Inflammatory Markers in Male and Female Patients with Covid-19
Differential White Cell Count in Male and Female Patients with Covid-19

	Male	Female	Total	p-value
D-dimers	1.1650(2.70)	1.12(4.01)	1.13(3.24)	0.797
CRP	74(154.00)	27.28(89.11)	48.50(120.54)	0.013
Ferritin	635.93(766.00)	361.00(606.00)	607.00(754.50)	0.024
LDH	349.00(357.15)	321.00(555.00)	348.00(388.00)	0.819
Total Leukocyte Count_IQR	11.64(5.91)	11.02(7.23)	11.27(6.49)	0.542
Neutrophil Count_IQR	79(21.0)	70(25.0)	77(22.0)	0.366
Lymphocyte Count_IQR	13(10.0)	14.0(19.00)	14(12.25)	0.283
NLR	5.85(6.66)	5.33(8.77)	5.85(7.77)	0.358

due to COVID-19 infection in six different tertiary care hospitals of Lahore. Patients with certain demographic characteristics were observed as more susceptible to Covid-19 infection such as older age group, patients with diabetes, hypertension and ischemic heart disease.

A retrospective study conducted on 200 patients in New York by Palaiodimos L, et al.⁷ also had median age of 64 years and in our study the median age of the patients was 58 years which is highly comparable with the study by Palaiodimos L, et al.⁷

Palaiodimos L, et al.⁷ revealed that the most common symptoms at presentation were Fever which was seen in (86%) cases, cough (76.5%), dyspnea (68%) of the cases comparing the results of this study with our study, we had fever, shortness of breath and cough with 80.4%, 63.0% and 57.6% percentages respectively and almost matching with the landmark study conducted in New York.

Palaiodimos L, et al.⁷ found out that Hypertension, hyperlipidemia and coronary artery disease was observed in (76%), (46.2%) and (16.5%) of their patients, respectively. Diabetes was prevalent in 39.5% of their admitted patients and (17%) had a history of heart failure while 27.5% had a history of asthma or COPD. 29% had a history of chronic kidney disease or end stage renal disease (ESRD) where as we found Diabetes mellitus as the most common type of comorbidity in our patients and was seen in 50% of the all cases, followed by hypertension and

Coronary heart disease in 44% and 17% respectively. These differences can be explained on the basis of the fact that we have more number of diabetes mellitus patient in this thickly populated city of Lahore and diabetes is the major risk factor for having hypertension and these two conditions, if uncontrolled which is the usually case in our country, in turn lead to development of ischemic heart disease.

A study by Bonetti G, et al.¹¹ and colleagues revealed the median age of 62 years of patients as compared to our study where the median age of the participants was 58 years which is highly comparable with our study.

A study Published in Cambridge University press in October 2020 by Malenfant JH, et al.¹² revealed that the most common initial symptoms observed were cough (51%), fever (41%), and myalgia (38%) and in our study the commonest symptoms observed were fever, shortness of breath and cough with 80.4%, 63.0% and 57.6% percentages respectively, which is highly comparable with our study in regard to cough and minor differences in other symptoms can be attributed to the fact that the study by Malenfant JH, et al.¹² only observed symptoms in health care workers

only.

A retrospective study conducted by Sanyaolu A and colleagues¹³ that most common comorbidities among COVID-19 deaths in United states of America was Hypertension in (55.4%) followed by diabetes mellitus in (37.3%), Hyperlipidemia in (18.5%) and coronary artery disease in (12.4%) Whereas in our study Diabetes was the most prevalent pre-existing condition with 29% men and 21% women known to have the disease. Hypertension followed the diabetes, this can be attributed to the fact that as south east Asians esp Pakistani has higher prevalence of diabetes mellitus so it came out to be the most common co morbidity in our population.

A Prospective multicenter study Conducted in South Africa by Calligaro GL, et al.¹⁴ revealed that high flow nasal oxygen was associated with better outcomes and patients were treated successfully and averted intubation too and their every patient was on 15 liters of oxygen before high flow nasal oxygen (HFNO) and the median (IQR) ratio of partial pressure of oxygen PaO_2 / fractioned inspired oxygen FiO_2 pre-HFNO was 68 (54–92), it is comparable with our study as well. Calligaro GL, et al.¹⁴ also revealed that diabetes (46%) was the most common co morbidity and comparing it our study we had 50% patients in total who had diabetes so highly comparable with our study.

A retrospective study conducted in Wuhan, China by Liao D and colleagues¹⁵ revealed that there was higher incidence of thrombocytopenia in patients who were critically sick (42 [49%] of 86) along with decreased lymphocytes and eosinophils in ICU treated participants. D-dimer, and fibrin degradation products (FDPs) were found to be strikingly high and correlated the disease severity and there was increased mortality with higher neutrophil to lymphocyte ratio (NLR) When we compare these results with our study we also had higher NLR in critically sick patients and also had significantly raised D-dimer in critical patients so it is highly comparable with our study.

Over 195 countries have been hit badly with COVID-19, resulting in millions of death worldwide and world's economy has been damaged quite badly along with religious, social and sports activities have been affected on larger scale and so the routine activities as well, As cases escalating globally, it has been observed in national and international studies that persons with underlying co-morbidities get prey of this deadly virus once it gets inside these individuals, they become severely ill as compared to people who have no co-morbid condition at all.

Due to SARS CoV-2, Novelty of this virus makes it unique, the proper understanding of the disease and

data regarding its course is scarce. It had been observed that patients with multiple comorbidities have more devastating/deadly outcomes compared with patients with one or no comorbidity. In our study COVID-19 patients who were already diagnosed case of diabetes, hypertension were badly affected along with grave outcomes and in literature too these two co-morbidities tops the list and talking about other conditions like obesity, chronic lung disease, and cardiovascular disease have poorer prognosis as well and lead to Acute respiratory distress syndrome (ARDS) and lethal pneumonia. Also, elderly patients having renal impairment and patients having different cancers are not only at risk for catching the virus easily, but also there is likely chance that their chances of survival goes down and remains a mystery.

Observations & Recommendations:

Symptoms of COVID-19 are diverse and are identified from trivial upper respiratory symptoms to severe disease leading patients to land in critical care area, leading to intubation and mechanical ventilation. Asymptomatic transmission is known entity and very dangerous too as persons would be infected and they will be unaware of it and can easily transmit the disease to others, so it is the need of the day to wear mask and observe social distancing religiously and avoid large gatherings and crowded public areas and norms of sneezing and coughing should be highlighted and dissipated to all communities through social and print media and that if someone develops respiratory symptoms, one must seek immediate health care services to avoid worse outcomes.

Therefore, patients with comorbidities and other persons too should take all necessary precautions to avert catching the SARS CoV-2, as they usually leads to worst end results with higher mortality. These precautionary measures include frequent hand-washing and using hand sanitizer, limiting person-to-person contact. So it is the need of the day to hold online symposia and raise awareness among general public through print and electronic media, on decreasing the load and frequency of the patients with these comorbid conditions and so the mortality in COVID-19-infected patients.

Conflict of Interest

None

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None

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