

The Dynamic Association between COVID-19 and Chronic Disorders: An Updated Insight into Prevalence Mechanism and Therapeutic Modalities

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Abstract

Covid-19 has emerged in December 2019 from the Wuhan city of china as a fatal disease with the drastic outcome which dreadfully affects life at the global level. The objective of this study is to determine the association of the chronic disease with covid-19. This cross-sectional based study was conducted at Shalimar hospital Lahore, Pakistan from May to July 2020. Total of 424 participants including 74 females and 350 males. The obtained results show that males are more susceptible to covid-19 and the life of patients with pre-existing chronic disease is more at risk than a healthy person. Statistically, the average age of patients is 50 with OR (1.751) (CI 1.32-1.71), a p-value less than 0.01, and the OR value of males is high than females that show males had a greater association with the covid-19 disease than females. Similarly, hypertension patients (41.9%) and diabetes (32.54%) had a substantial association with covid-19, OR (0.354), CI 1.95-1.98, and OR (0.322), CI 1.27-2.23 respectively. Chronic liver disease was found in 13.44% (OR=1.89, CI=1.45-1.55) patients, heart disease 8.72% (OR=0.145, CI=1.23-1.25) and cancer 3.3% (OR=0.121, CI= 1.27-1.33) with a p-value greater than 0.01. The OR values indicated that chronic disorder has a significant association with covid-19 and evidence of the mechanism of action shows that covid-19 has the ability to develop a chronic disease. However, we concluded that its lethal effects also depend on the patient's disease status.

Keywords: Covid-19, chronic liver disorder, hypertension, cardiovascular disease, diabetes

Introduction

Covid-19 is a disease that has emerged as public health challenges with clinical symptoms of fever, cough, fatigue, and breathing difficulties.¹⁷ This disease rapidly spread out from Wuhan city of China to the world and later identified as a respiratory syndrome. Due to its transmission from human to human and worldwide rapidly spread of the infection, WHO declared coronavirus disease as pandemic on March 11, 2020.¹⁸ SAR-Cov-2 has the resemblance with the genus Betacoronavirus and 80% with SAR-Cov.¹⁹ After some time virus come out with fatal complications such as sudden organ failure, pulmonary oedema, severe pneumonia, and acute respiratory distress syndrome (ARDS).²⁰ The data at the beginning months of outbreak shows the high prevalence rate in patients with chronic disease including cardiovascular, diabetes, respiratory, and kidney disease.²¹ A retrospective study reported that 138 patients were infected with covid-19, concluded that 64 patients were suffering from underline disorders and 23 patients were admitted to the intensive care unit (ICU).²² Almost 72.2% of patients admitted in ICU were older, had underlying comorbidities and dyspnea, many (47.7%) of them were at the ventilator. The outcomes of these studies are the obvious indication like age and chronic disease are major factors that contribute to the fatality of Covid-19 disease. A functional receptor Angiotensin-converting enzyme 2, facilitate the virus to cellular level²³ and strength of ACE2 expression elucidates the disease severity inpatient. The disease severity can also be identified through excessive immune reaction namely as a cytokine storm.²⁴ surprisingly, few cases were reported the sudden damage of orange after the onset of disease in patients without a previous history of chronic disease and it might be because of myocardial injury, acute diabetes, GIT complications and liver-related chronic complications.²⁵

Methods

This cross-sectional study was conducted at Shalimar hospital Lahore, Pakistan from May to July 2020. The clinical and laboratory data of 424 patients (at least with one chronic disease e.g. cardiovascular, diabetes, and liver disease) of age greater than 18 years were admitted at hospital were collected. We obtained oral consent

from all the patients included in the study. All the participants have diagnosed with positive Covid-19 and the diagnosis of covid-19 was based on guidelines set by the Shalimar hospital followed according to pandemic condition and as per WHO guidelines for disease control and prevention. The study excluded pregnant women and children.

Grading criteria

The grading criteria based on the patient's symptoms, laboratory results with imaging findings and disease severity can discriminate into mild, moderate, severe, and critical. When patients with mild symptoms without findings of pneumonia are treated as mild infection conditions. If patients show fever and difficulty in breath are considered as moderate condition, patients with respiratory rate are greater than 30/minute, blood oxygen saturation is less than 93% such patients are with a severe condition. Patients with critical condition needed mechanical ventilation, shocks, and failure of other organs (as in case of pre-existing chronic disorders) required ICU therapy.

Mechanism of covid-19 to develop chronic disease complications

The virus attacked the cardio-myocytes lead to develop cardiovascular complications. First virus the lungs and assail pulmonary artery vascular cells through which it moves towards the heart and targets the heart muscles. Elevate the level of angiotensin-converting enzyme 2 (ACE-2) which boost the virus attack and injure the heart muscles.⁷ this condition flood with inflammatory cytokines which activates the T-helper-1 cells, further enhance the inflammatory cytokines, more harmful to the heart.⁸

In the case of acute respiratory disease, covid-19 affects the epithelial lining of alveoli lead to direct pulmonary injury, through ACE-2 expressing pneumocytes, and patients were found with diffused alveolar damaged in lungs¹⁰. Pro-inflammatory cytokines were released by cytokine storms which aggressively damages the lungs.⁹

In an infected person liver ample with ACE2 particularly on the surface of hepatic endothelial cells. Covid-19 infects the liver greater than lungs as ACE2 factor is largely found in bile duct than liver cells while expression is the same as the alveolar cells of the lungs.¹² Therefore in the case of covid-19 liver injury is because of the damaged bile duct instead of hepatocytes. Notably, respiratory failure in covid-19 patients is due to liver injury. The escalating level of inflammatory cytokine significantly damaged the liver.¹¹

Statistical analysis

All the data were statistically analyzed using the SPSS version 23. The association of chronic disease based on the severity level was determined through the multivariate logistic regression assay including 95% confidence interval and odd ratio (OR) and p-value less than 0.01 indicate the significant relation and p-value greater than 0.01 indicates the non-significant relation.

Results

Results of table 1 presenting the common symptoms and vital signs of all the patients contributed to the study. The majority had a fever (77.5%), cough (70.9%), and dyspnea (74%). One out of 6 patients had nausea/vomiting (23.3%) and diarrhea (21.2%). A tiny percentage of patients with anosmia (4.95%), ageusia (5.4%), and myalgia (10.3). The male patients had a substantially greater percentage of fever and diarrhea than female patients with a p-value of 0.02 and 0.03. Assessment of vital signs indicates that's the respiratory rate was worse in males as compared to females with the p-value 0.02.

Multivariate logistic Regression analysis results were given below in table 2 which revealed that the average age of patients is 50 with OR (1.751) (CI 1.32-1.71), a p-value less than 0.01, and OR value of males is high than females that show males had a greater association with the covid-19 disease than females. Similarly, hypertension patients (41.9%) and diabetes (32.54%) had a substantial association with covid-19, OR (0.354), CI 1.95-1.98, and OR (0.322), CI 1.27-2.23 respectively. Chronic liver disease was found in 13.44%

(OR=189, CI=1.45-1.55) patients, heart disease 8.72% (OR=0.145, CI=1.23-1.25) and cancer 3.3% (OR=0.121, CI= 1.27-1.33) with a p-value greater than 0.01. Thus, Covid-19 association with chronic disease depends on the severity of the disease which is described in table 3.

Table. 3 present the patients with severity of disease 74 patients are females out of 424 where 50 (67%) female patients were with mild to moderate disease, 20 (27%) with severe symptoms and 4(5.4%) female patients at critical stage. Total male patients were 350 (82%) out of 424 and out of 350 male patients 200 (57.1%) are with mild to moderate symptoms, 91 patients (26%) with severe disease, 59 (16.8%) patient were at critical phase. Out of 424 patients 178 (41.9%) patients were with hypertension (in these patients 60% = mild to moderate, 61% = severe case and 5% critical stage). 138 (32.5%) patients with diabetes (out of 138 patients, 89 (64.4%) = mild to moderate, 36 (26%) = severe, 13 (9.42%) = critical). 57 (13.44%) patients with chronic liver disease (34 (59.64%) patients = moderate to mild disease, 13 patients (22.8%) = severe, 10 (17.5%) patients = critical) with p-value 0.001. 37 (8.72%) patients with heart disease (20% cases = moderate, 24.3%= severe, 21.62% = critical). 14 (3.3%) patients with cancer (64.28% = mild to moderate, 14.2% = severe cases, 21.42% = critical) with p-value 0.003.

Management of chronic disease with covid-19

Covid-19 infected patients with liver disorder need intense care and preventive measures to protect the liver from more damage. Critical monitoring of liver biochemistry and do the screening of patients with hepatitis B or C and treated with antiviral therapy.¹³

Immune modulating agents used to manage cardiovascular disease. The monoclonal antibodies, tocilizumab blocked the interleukins-6 receptors which help in the reduction of myocardial inflammation. IV immunoglobulins were considered valuable to manage myocardial disease.¹⁴ American heart association and the European society of cardiology does not encourage to prescribe of non-steroidal anti-inflammatory drugs.

A study of respiratory disorder reported the reduction in ACE2 expression level with the use of inhaled corticosteroid, results of the study indicate the dose-dependent relationship with the molecular phenotype of asthma.¹⁶ In a controlled trial based study alteration in genes of SARS-CoV-2 was reported with inhaled corticosteroid treatment. The consumption of anti-asthmatic medication has an anti-inflammatory effect such as Leukotriene modifier (montelukast), help in the reduction of the level of pro-inflammatory cytokine and interleukins-6, thus it brings down the storm of cytokine in patients of covid-19.¹⁵

Table.1 Common symptoms and signs of Covid-19 in patients

Parameters	Patients n=424	Males n= 350	Females n= 74	p-value
Symptoms				
Fever (%)	329 (77.5)	249 (71.1)	49 (66)	0.02
Cough (%)	301 (70.9)	211 (60)	50 (67)	0.43
Dyspnea (%)	314 (74)	226 (64.5)	48 (64.8)	0.72
Nausea/ vomiting (%)	99 (23.3)	78 (22.2)	25 (33.7)	0.62
Diarrhea (%)	90 (21.2)	81 (23.1)	19 (25.6)	0.03
Anosmia (%)	21 (4.95)	15 (4.2)	9 (12.1)	0.32
Ageusia (%)	23 (5.4)	17 (4.8)	8 (10.8)	0.43
Myalgia (%)	44 (10.3)	28 (8)	12 (16.2)	0.72
Vital symptoms				
Temperature (°C)	37.6 ± 0.9	37.6 ± 0.8	37.8 ± 0.9	0.45
Heart rate (beat/minute)	95.7 ± 16.9	96.5 ± 15.6	97.7 ± 17.9	0.11
Respiratory rate (breath/minute)	24.9 ± 8.7	25.6 ± 9.6	23.6 ± 5.7	0.02
Systolic blood pressure (mmHg)	126 ± 18.7	125.8 ± 19.6	124.6 ± 19.8	0.71
Diastolic blood pressure (mmHg)	72.7 ± 12.9	73.5 ± 11.4	71.1 ± 11.8	0.52
SpO ₂	91.0 ± 6.9	91.0 ± 2.7	90.6 ± 5.6	0.35

Table.2 The association of different chronic disease with the covid-19 patients

Characteristic	Number of patients n=424	Percentage	Odd ratio (OR)	95% confidence interval (CI)	P-value
Age mean (SD)	50 (12)	-----	1.751	1.32-1.71	0.002
Females	74	17%	0.185	0.28-1.00	-----
Males	350	82%	0.486	1.45-1.20	-----
Hypertension	178	41.9%	0.354	1.95-1.98	0.003
Diabetes	138	32.54%	0.322	1.27-2.23	0.024
Chronic liver disease	57	13.44%	0.198	1.45-1.55	0.014
Heart disease	37	8.72%	0.145	1.23-1.25	0.035
Cancer	14	3.3%	0.121	1.27-1.33	0.032

Table.3 Baseline characteristic of 424 patients infected with covid-19

Characteristic	Number of patients n=424	Mild to moderate disease	Severe patients	Critical patients	P-value
Age mean (SD)	50 (12)			0.060	
Females	74 (17%)	50 (67%)	20 (27%)	4 (5.4%)	-----
Males	350 (82%)	200 (57.1%)	91 (26%)	59 (16.8%)	-----
Hypertension	178 (41.9%)	108 (60%)	61 (34.2%)	9 (5%)	0.035
Diabetes	138 (32.5%)	89 (64.4%)	36 (26%)	13 (9.42%)	0.024
Chronic liver disease	57 (13.44%)	34 (59.64%)	13 (22.8%)	10 (17.5%)	0.014
Heart disease	37 (8.72%)	20 (54%)	9 (24.3%)	8 (21.62%)	0.001
Cancer	14 (3.3%)	9 (64.28%)	2 (14.2%)	3 (21.42%)	0.003

Discussion

Globally, covid-19 affect a huge number of population. The ratio of infected males is observed greater in our study than females and demonstrated that males are vulnerable to covid-19. However, the similarity was found in clinical symptoms for both sexes as mention in table 1. Generally included fever, cough, fatigue, breathing difficulty, and diarrhea. Moreover, a study illustrated that diarrhea was found in 21% of patients with covid-19 and older patients easily develop chronic disease as compared to patients without diarrhea. Thus, diarrhea may be one reason to develop disease severity.¹ Another, study shows that older age persons are at higher risk of death due to seasonal and pandemic influenza as compare to children and Youngers aged <18 years, substantially lower the risk of death during the pandemic.²

In our study percentage of diabetes (32.54%), chronic liver disease (13.44%) is much less than hypertension patients (41.9%) which suggested that the prevalence of hypertension disease is higher than other chronic diseases. A recent study shows that one-third of 32.5% of Chinese adults had developed hypertension and the occurrence rate of other diseases namely diabetes, coronary heart disease, and chronic pulmonary disorders were 10.4%, 1.03%, and 8.0%. Therefore, we concluded that hypertension is more common in the general population and the incidence of hypertension is also substantially higher in patients with covid-19.³

A study attempted to note the patients with the chronic pulmonary disease were required the ICU treatment and ventilator support if they got infected with pandemic disease covid-19.⁴ Patients with pulmonary disorder likely more susceptible to develop severe cases of covid-19.⁵ The prevalence of covid-19 is around 50% in

hypertension and diabetes, and 30% in CVD patients.⁶ In this study we found a potent association of chronic disease with disease severity. In previous studies, we found many data about the correlation of pre-existing chronic disease and few studies were without the pre-existing chronic disease.

Conclusion

The covid-19 pandemic has widely damaged the world with a huge number of morbidity and mortality. This newly emerged disease has not been studied yet from every aspect, as diversity was found which affects almost every organ of the body differently. Therefore, its mechanism of action on the human body is not exactly known. We have no cure and vaccine in our hands. However, in our study, we concluded that it can propel towards chronic disorders and people with pre-existing chronic disease is more susceptible to this infection. More evidence is required to make sure its cure using the existing medicine.

References

- i. Wan Y, Li J, Shen L, Zou Y, Hou L, Zhu L, et al. (2020). Enteric involvement in hospitalised patients with COVID-19 outside Wuhan. *Lancet Gastroenterol Hepatol*, in press.
- ii. Mertz D, Kim TH, Johnstone J, Lam P-P, Science M, Kuster SP, et al. (2013). Populations at risk for severe or complicated influenza illness: systematic review and meta-analysis. *BMJ*, 347: f5061.
- iii. Grasselli Giacomo, Zangrillo Alberto, Zanella Alberto, Antonelli Massimo, Cabrini Luca, Castelli Antonio, et al. (2020). Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA*, in press.
- iv. Lewington S, Lacey B, Clarke R, Guo Y, Kong XL, Yang L, et al. (2016). The burden of hypertension and association risk for cardiovascular mortality in China. *JAMA Intern Med*. 176:524-532.
- v. Wang B, Li RB, Lu Z, Huang Y (2020). Does comorbidity increase the risk of patients with COVID19: evidence from meta-analysis. *Aging*, in press.
- vi. Badawi A, Ryoo SG (2016). Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. *Int J Infect Dis*, 49:129-133.
- vii. Guo, J., Wei, X., Li, Q., et al., 2020. Single-cell RNA analysis on ACE2 expression provides insights into SARS-CoV-2 potential entry into the bloodstream and heart injury. *J. Cell. Physiol*. 235, 9884–9894.
- viii. Siripanthong, B., Nazarian, S., Muser, D., et al., 2020. Recognizing COVID-19-related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management. *Heart Rhythm*. 17 (9), 1463–1471.
- ix. Chousterman, B.G., Swirski, F.K., Weber, G.F., 2017. Cytokine storm and sepsis disease pathogenesis. *Semin. Immunopathol*. 39 (5), 517–528.
- x. Zhang, H., Penninger, J.M., Li, Y., Zhong, N., Slutsky, A.S., 2020b. Angiotensin converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. *Intensive Care Med*. 46 (4), 586–590.
- xi. Sun, J., Aghemo, A., Forner, A., Valenti, L., 2020. COVID-19 and liver disease. *Liver Int*. 40 (6), 1278–1281.
- xii. Chen, D., Li, X., Song, Q., et al., 2020e. Assessment of Hypokalemia and Clinical Characteristics in Patients With Coronavirus Disease 2019 in Wenzhou, China. *JAMA Netw Open*. 3 (6), e2011122
- xiii. Boettler, T., Newsome, P.N., Mondelli, M.U., et al., 2020. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper. *JHEP Rep*. 2 (3), 100113.
- xiv. Siripanthong, B., Nazarian, S., Muser, D., et al., 2020. Recognizing COVID-19-related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management. *Heart Rhythm*. 17 (9), 1463–1471.
- xv. Fidan, C., Aydogdu, A., 2020. As a potential treatment of COVID-19: Montelukast. *Med. Hypotheses* 142, 109828.
- xvi. Petrosillo, N., Viceconte, G., Ergonul, O., Ippolito, G., Petersen, E., 2020. COVID-19, SARS and MERS: are they closely related? *Clin. Microbiol. Infect*. 26 (6), 729–734.

- xvii. Bajgain, K.T., Badal, S., Bajgain, B.B., Santana, M.J., 2020. Prevalence of comorbidities among individuals with COVID-19: A rapid review of current literature. *Am. J. Infect. Control*.
- xviii. WHO, 2020 Jul 18 2020. Clinical management of COVID-19 interim guidance 2020. Updated May 27 2020; cited. Available from: [https://www.who.int/publications/i/item/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications/i/item/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected).
- xix. Sharma, A., Tiwari, S., Deb, M.K., Marty, J.L., 2020. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2): a global pandemic and treatment strategies. *Int. J. Antimicrob. Agents* 56 (2), 106054.
- xx. Chen, N., Zhou, M., Dong, X., et al., 2020a. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 395 (10223), 507–513.
- xxi. Guan, W.J., Liang, W.H., Zhao, Y., et al., 2020a. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur. Respir. J.* 55 (5), 2000547.
- xxii. Wang, B., Li, R., Lu, Z., Huang, Y., 2020b. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. *Aging (Albany NY)* 12 (7), 6049–6057.
- xxiii. Chu, H., Chan, J.F., Yuen, T.T., et al., 2020. Comparative tropism, replication kinetics, and cell damage profiling of SARS-CoV-2 and SARS-CoV with implications for clinical manifestations, transmissibility, and laboratory studies of COVID-19: an observational study. *Lancet Microbe*. 1 (1), e14–e23.
- xxiv. Abdin, S.M., Elgendy, S.M., Alyammahi, S.K., Alhamad, D.W., Omar, H.A., 2020. Tackling the cytokine storm in COVID-19, challenges and hopes. *Life Sci.* 257, 118054.
- xxv. Grasselli, G., Zangrillo, A., Zanella, A., et al., 2020. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region. *Italy. JAMA*. 323 (16), 1574–1581.