ORIGINAL ARTICLE

Factors Associated with Duration of Hospitalization in Patients with COVID-19

Zi-Ang Li[1], Jun Lin[2]

ABSTRACT

Background and Objective: Coronavirus disease 2019 (COVID-19) has caused a large number of casualties and economic losses. Reducing the number of hospitalization days can alleviate pressure on health services and save more people. This study was carried out to find associated factors with the duration of hospitalization at a COVID-19 dedicated hospital in China.

Methods: In this retrospective study, the demographic details and laboratory tests of 556 patients were collected. These patients were cured and discharged. The data was analyzed using statistical package for the social sciences (SPSS), version 22. The Shapiro-Wilk method was used for the normality of data with $P \leq 0.05$ as significant to relate factors with the duration of hospitalization.

Results: A total of 556 patients with COVID-19 were included in the study; 249 were males and 307 were females. Among the factors associated with longer hospital stay, lower K+ and Na+ levels were noticed in 102 (18.5%) and 61 (11%) respectively. Among liver functions tests, elevated AST levels was found in 109 (19.6%) patients, decreased serum albumin seen in 301 (54.1%) patients, elevated serum ALT levels in 80 (14.3%) patients with longer hospital stay ($P = 0.032$). Increased procalcitonin (PCT) was noticed in 66 (11.8%) patients. An elevated level of plasma D-dimer was seen in 125(22.4%) and increased NT-pro BNP levels in 64 (11.5%) patients. Increased cTnT levels were found in 76(13.6%) patients and elevated creatinine levels in 114 (21%) patients.($P = 0.015$).

Conclusion: Patients with elevated serum total cholesterol had significantly lesser hospital stay than the normal group. Patients with temperature ≥ 38°C and elevated blood glucose had longer hospitalization stay. We recommend that health care providers should not ignore multiple organ support when treating patients.

KEYWORDS: Coronavirus disease 2019, Hospitalization, Organ function, Infectious disease.

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INTRODUCTION

On 14th August 2020, the globally infected patients of COVID-19 had exceeded more than 20 million and more than 0.7 million people lost their lives.[1] Most of the recent research has focused on discussing indicators related to mortality.[2,3] Mortality can reflect both the severity of the disease and the ability of the medical system to respond to such health emergencies. For the entire patient population, the mortality rate is one of the evaluation indices but does not evaluate the non-fatal cases; cured and discharged after treatment.

Hospital stay is one of the best indicators for evaluating cured patients. Because the length of hospitalization can reflect the comprehensive treatment effect, as well as the patient's medical cost (the longer the hospitalization time, the higher the medical expenses). Existing clinical trials of Lopinavir-Ritonavir also used the length of hospital stay as one of the indicators to evaluate the efficacy of the drug.[4]

Reducing the length of hospital stay is important because it may alleviate the pressure of extreme shortage of medical resources and funds. Therefore, this study retrospectively analyzed data from a single center in Wuhan, China, to explore factors that are potentially associated with length of hospital stay in COVID-19 patients who were cured and discharged from hospital. These factors may help the health care professional to take measures to reduce the number of hospitalization stay so that medical resources can be fully utilized.

METHODS

This retrospective study included 556 cured COVID-19 patients who received treatment in the Zhongnan Hospital of Wuhan University, China from 15th December, 2019 to 14th March, 2020. This hospital is a designated to treat patients with COVID-19 and supervised by the Zhongnan Hospital of Wuhan University, China. The diagnosis, classification, treatment and discharge criteria of patients in this study were based on the new coronavirus pneumonia diagnosis and treatment plan (7th edition).[5] The ethics committee of Zhongnan Hospital of Wuhan University, China, believes that this study does not involve patient intervention and follow-up or breach of patients' confidentiality, hence it was exempted from Instituitonal Ethical Approval.

The laboratory confirmed COVID-19 patients by Polymerase chain reaction (PCR), who were cured and discharged, having age ≥ 18 years, were included. Transfer, death of patient and the patients with incomplete data on history and analysis, were the reasons of exclusion. Following 24 indicators were considered in this study: gender, age, body temperature at admission, the first laboratory examination at admission (procalcitonin (PCT), hemoglobin, platelets, red blood cell, white blood cell, serum albumin, serum total bilirubin, alanine transaminase (ALT), aspartate aminotransferase (AST), cardiac troponin T(cTnT), NT-pro BNP, glomerular filtration rate, serum creatinine, blood K+ level, blood Na+ level, serum total cholesterol, serum triglycerides, activated partial thromboplastin time (APTT), international normalized ratio (INR), prothrombin time (PT), D-dimmer, blood glucose). It is worth mentioning that these indicators (temperature measurement and blood collection) are completed within the first day of hospitalization.

STATISTICAL ANALYSIS

Statistical analysis was performed using statistical package for the social sciences (SPSS), version 22 software. Continuous numeric variables were expressed in mean ± standard deviation (SD). The Shapiro-Wilk method was used for the normality of data with P-value ≤ 0.05, taken as significant. The F-test (Levene's test) was used for the homogeneity of variance. The independent students' T-test was used for the data that met the normal distribution and variance homogeneity and the Mann-Whitney U test was used for the data that did not satisfy the normal distribution and homogeneity of variance.

RESULTS

The baseline data of patients is listed in Table-1. The average days of hospital stay were 17.44 ± 9.788. Among 556 patients with COVID-19 there were 249 males and there was slight female preponderance, as 307 patients were females. Of the factors associated with longer hospital stay, among electrolytes; lower K+ and Na+ levels were noticed in 102(18.5%) and 61(11%) respectively. (Fig.1). Among liver functions tests elevated AST levels was found in 109(19.6%) patients, decreased serum albumin seen in 301(54.1%) patients, elevated serum ALT levels in 80(14.3%) patients with longer hospital stay, P = 0.032 (Fig.2). Increased procalcitonin (PCT) was noticed in 66 (11.8%) patients, elevated plasma D-dimmer was seen in 125 (22.4%), elevated PT in 118 (21.2) patients, decreased platelets in 52 (9.35%) patients, increased INR in 14 (2.51%) patients, increased NT-pro BNP levels in 64 (11.5%) patients, increased cTnT levels in 76 (13.6%) patients and elevated creatinine levels in 114

(21%) patients having significant P-value (P = 0.015). Interestingly, patients with elevated total serum cholesterol (P = 0.014) had significantly less days of hospital stay. The increase in PCT, which is an indicator of infection, caused longer days, but the increase in white blood cells has nothing to do with it (Fig.3). In terms of coagulation function, the number of hospitalization days in patients with elevated plasma D-dimmer (P < 0.001), PT (P < 0.001) and INR (P = 0.001) increased significantly, but there was no difference in the increase in APTT in these patients (Fig.4). In cardiac function indexes, patients with increased NT-pro BNP level (P < 0.001) and cTnT (P < 0.001) level had longer hospital stay. In renal function, increased blood creatinine level (P = 0.015) has longer hospital stay, while decreased glomerular filtration rate cannot affect hospital stay (Fig.5). There was no difference in the length of hospital stay for patients with reduced red blood cells, white blood cells, and hemoglobin. However, the decrease in platelets (P < 0.001) significantly increased the number of hospital stay (Fig.6). The results of other indicators showed that patients ≥ 65 years old had longer hospital stay than patients < 65 years old (P < 0.001), men had longer hospital stay than women (P = 0.0081), and patients who measured body temperature ≥ 38°C at admission had more days of hospitalization. Patients who had elevated random blood glucose levels for the first time on admission had a longer hospital stay (P < 0.001) (Fig.7).

Table-1: Associated factors of patients with COVID-19 related to hospital stay

	Number of patients (n)	*Hospital duration (in days) (Mean ± SD)*
Total:	556	17.44 ± 9.788
Mild symptoms	2	19 ± 0
Moderate symptoms	363	16.28 ± 9.706
Severe symptoms	185	19.35 ± 9.382
Critical patients	6	28.5 ± 13.882
Gender:		
Male	249	18.6506 ± 10.17044
Female	307	16.456 ± 9.36761
Age		
≥ 65	174	19.7011 ± 10.52453
< 65	382	16.4083 ± 9.26545
Temperature:		
≥ 38	39	21.5897 ± 9.89077
< 38	468	17.1218 ± 9.63199
PCT: (0 ~ 0.1 ng/ml)		
Elevation	66	22.9091 ± 10.41113
Normal	249	16.8514 ± 9.8463
Hemoglobin: (115 ~ 150g/L)		
Normal	337	17.7834 ± 9.88102
Reduction	111	17.1081 ± 9.95476
Platelets: (125 ~ 350 10^9/L)		
Normal	391	16.6624 ± 9.68232
Reduction	52	24.1538 ± 9.87448
Red blood cell: (3.8 ~ 5.1 10^12/L)		
Normal	357	17.7339 ± 9.78931
Reduction	76	17.4605 ± 10.84121
White blood cell: (3.5 ~ 9.5 10^9/L)		
Normal	369	17.1436 ± 9.79122
Reduction	70	19.2286 ± 9.66117
Elevation	31	19.5806 ± 11.36009
Serum albumin: (40 ~ 55 g/L)		
Normal	175	14.5314 ± 8.81273
Reduction	301	19.5515 ± 9.90496
Serum total bilirubin: (2 ~ 23 μmol/L)		
Normal	464	17.7026 ± 9.85587
Elevation	9	18.4444 ± 8.63295
ALT: (7 ~ 40 IU/L)		
Normal	384	17.5052 ± 9.89422
Elevation	80	19.6375 ± 9.52046
AST: (13 ~ 35 IU/L)		
Normal	338	16.6657 ± 9.42426
Elevation	109	21.7615 ± 10.09850
cTnT: (0 ~ 0.014 ng/ml)		
Normal	342	17.4357 ± 10.04361
Elevation	76	21.3947 ± 9.55556
NT-proBNP: (0 ~ 222 pg/mL)		
Normal	115	16.4783 ± 9.77766
Elevation	64	22.0313 ± 10.03481
Glomerular filtration rate: (66 ~ 143 ml/min)		
Normal	357	17.8459 ± 9.74946
Reduction	28	21.3571 ± 11.05948
Serum creatinine: (1 ~ 73 μmol/L)		
Normal	344	17.1047 ± 9.87948
Elevation	114	19.4035 ± 9.70423
Blood K+ level: (3.5 ~ 5.3 mmol/L)		
Normal	359	16.6769 ± 9.81712
Elevation	3	17 ± 2.64575
Reduction	102	21.2157 ± 9.32964
Blood Na+ level: (137 ~ 147 mmol/L)		
Normal	392	16.7015 ± 9.77262
Elevation	11	20.2727 ± 8.08815
Reduction	61	23.4754 ± 8.61318

Serum total cholesterol: (2.8 ~ 5.2 mmol/L)		
Normal	330	18.0394 ± 9.84816
Elevation	51	14.5098 ± 8.13234
Serum triglycerides: (0.56 ~ 1.7 mmol/L)		
Normal	303	18.1848 ± 10.03762
Elevation	71	15.8732 ± 8.76671
APTT: (24.6 ~ 35.4 s)		
Normal	319	17.9624 ± 10.08666
Elevation	64	18.7969 ± 10.40327
INR: (0.76 ~ 1.42)		
Normal	370	17.7973 ± 10.08068
Elevation	14	26.0714 ± 7.79017
PT: (9.3 ~ 12.9 s)		
Normal	265	16.3472 ± 9.87077
Elevation	118	22.0763 ± 9.59982
D-dimmer: (0 ~ 0.243 μg/mL)		
Normal	202	15.9554 ± 9.71858
Elevation	125	20.9280 ± 9.92892
Blood glucose: (3.9 ~ 5.8 mmol/L)		
Normal	210	14.7238 ± 8.59007
Elevation	220	20.7409 ± 9.92258

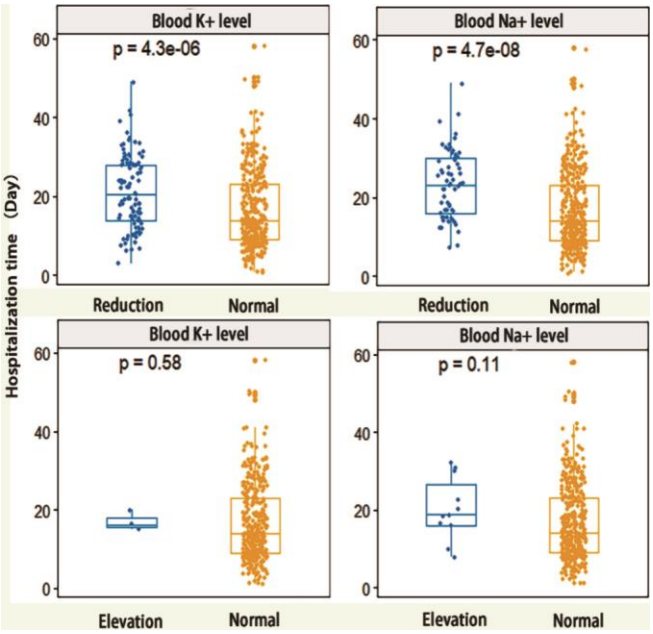

Fig.1: Hospitalization time of Na +, K + level, AST, ALT, serum total bilirubin and serum albumin.

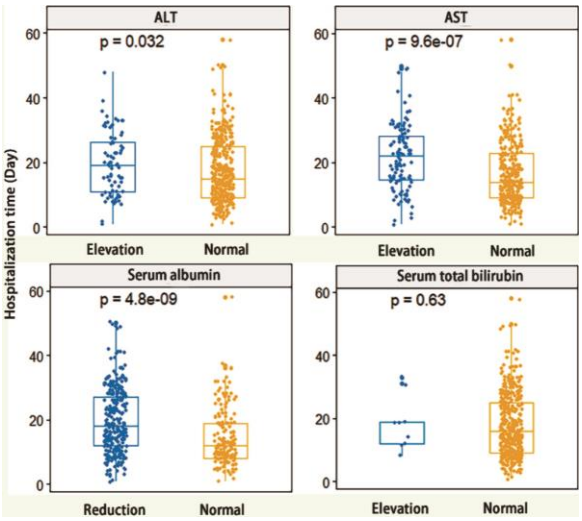

Fig.2: Hospitalization time of different group in AST, ALT, serum total bilirubin and serum albumin.

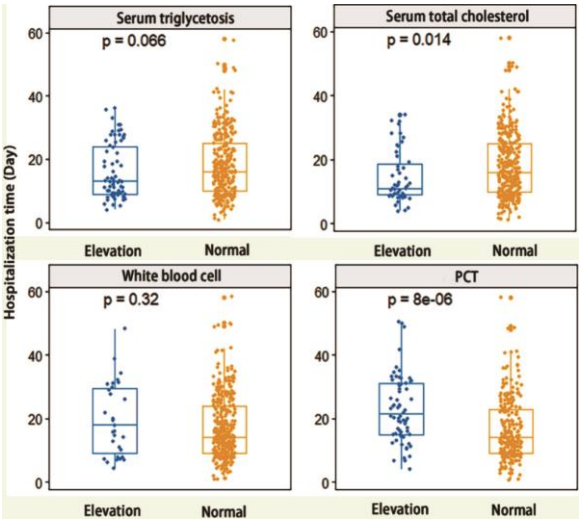

Fig.3: Hospitalization time in relation to infection, blood lipid index.

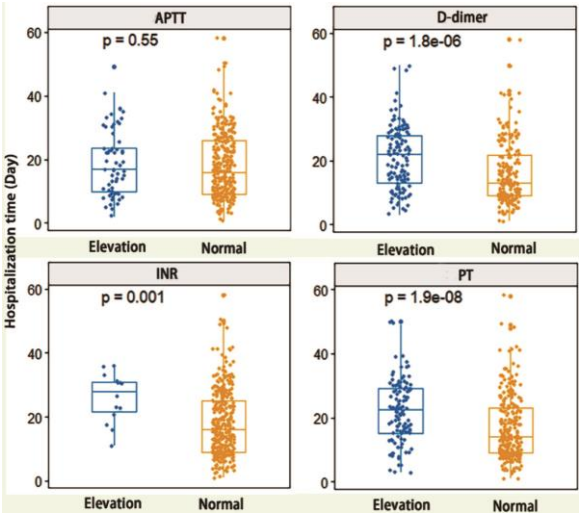

Fig.4: Hospitalization time in relation to D-dimers, PT, APTT and INR.

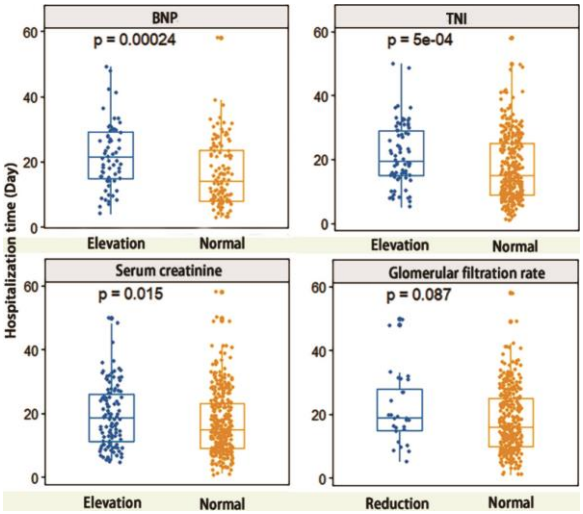

Fig.5: Comparison hospitalization time of different group in cardiac function, renal function.

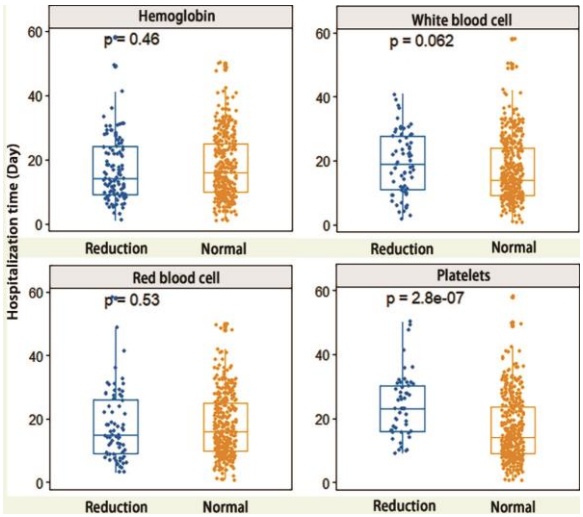

Fig.6: Hospitalization time of serum blood indexes.

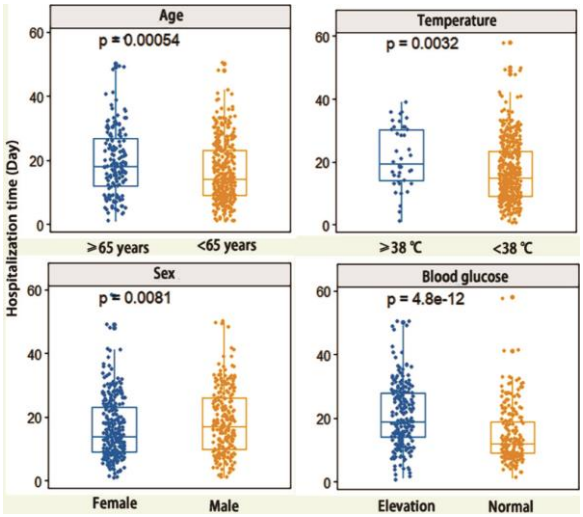

Fig.7: Hospitalization time in age, gender, blood glucose and body temperature.

DISCUSSION

The examination at the time of admission of the patient largely reflects the state of the disease at the early stage, and provides great help for the subsequent diagnosis and treatment. The result of this study shows that people with abnormal liver function indicators have longer hospital stay. The study by Zhang et al.[6] reported that 2-11% of COVID-19 patients have liver comorbidities, manifested by abnormal indicators such as AST, ALT, serum albumin, and the proportion of severe cases may be higher. This indicates that the liver may be closely related to the development of the disease. However, plenty of studies have reported abnormalities in laboratory tests, and there is currently insufficient evidence to show that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected liver cells or virus-related liver damage in COVID-19.[7] The authors recommend that in addition to the necessary antiviral treatment during hospitalization, patients with abnormal liver function should also actively carry out liver protection and enzyme-lowering therapy, and patients with normal liver function should be regularly monitored, which can more effectively treat patients. The increase in serum total bilirubin does not affect the length of hospitalization, which indicates that the biliary system may not be related to the progression of the disease.

In terms of coagulation function, the increase in plasma D-dimmer, PT and INR, and decrease in platelets can significantly increase the length of hospital stay. Elevated D-dimmer means that the patient's blood is in a hypercoagulable state, and an increase in PT and INR and a decrease in platelets indicate that the patient has a bleeding tendency. Li et al.[8] found that patients with SARS-CoV-2 infection have obvious coagulation abnormalities, which are manifested by increased D-dimmer, PT prolongation, fibrinogen (FBG) and platelets decreasing and DIC. Early treatment is very important. This shows that SARS-Cov-2 infection can make coagulation function worse. For COVID-19 patients, except for those who need to take anticoagulants for a long time due to primary disease, such as coronary heart disease, patients with abnormal coagulation function need necessary treatment, for example, patients with elevated D-dimmer can take anticoagulation treatments like

injecting low molecular weight heparin (LMWH). Patients with reduced Na+ and K+ had longer hospital stay, but there was no difference in the increase. The authors think it may be that the sample size of the elevated group is too small and the results are biased. In fact, it is not difficult to understand that the receptor of SARS-Cov-2, ACE-2, plays a very important role in the renin-angiotensin system (RAS). The RAS system can regulate the water and electrolyte balance, so COVID-19 patients with electrolyte disturbances should be very common, and the role of angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor-1 (AT1R) inhibitor in the treatment of COVID-19 disease has been discussed internationally.[9,10] In general, it is very necessary to correct patients' electrolyte disturbance during hospitalization. In addition, the current study also found an interesting result that the patients with elevated serum cholesterol significantly had reduced duration of hospital stay. Further studies may be required to find out the protective role of cholesterol in COVID-19 patients.

Patients with increased NT-pro BNP levels and cTnT levels; two important indicators of cardiac function, had longer hospital stay. Increased NT-pro BNP represents heart failure in the patient. Increased cTnT levels indicate that the patient's myocardium is damaged. The increase in the index at the time of admission means that SARS-Cov-2 has already had heart damage early. Studies by Shi et al.[11] and Li et al.[12] have found that SARS-Cov-2 can cause myocardial damage. For COVID-19 patients, treatment of heart failure, arrhythmia, acute coronary syndrome and thrombosis are very important.[13]

Patients with elevated blood creatinine had longer hospital stay, but decreased glomerular filtration rate did not affect hospital stay. SARS-Cov-2 may damage the kidneys based on the RAS system.[14] Research by Cheng et al.[15] showed that the prevalence of kidney disease at admission was high, mainly manifested by increased creatinine, increased blood urea nitrogen and decreased glomerular filtration rate, and the risk of death in hospital was higher. Although our results show that renal function does not seem to have a significant relationship with the length of hospital stay, a large number of studies have confirmed that abnormal renal function is closely related to COVID-19 disease. Therefore, treating abnormal renal function is of great significance to curb the development of the disease.

Other indicators such as age, gender, and body temperature are all related to the length of hospital stay. In addition, the number of hospital days for patients with elevated random blood glucose at admission was significantly increased. The angiotensin-converting enzyme-2 (ACE-2) receptor is expressed in the pancreatic islets, and it has been previously reported that severe acute respiratory syndrome coronavirus-1 (SARS-Cov-1) infected patients without diabetes developed diabetes.[16] Therefore, the damage of SARS-Cov-2 to islet cells cannot be ruled out. In addition, there is a lot of evidence that COVID-19 patients have an increased probability of developing diabetes, and controlling blood glucose is very helpful for controlling the disease.[17,18,19]

CONCLUSION

SARS-Cov-2 can cause damage to organ function throughout the body. Therefore, in addition to antiviral treatment, attention should also be paid to the recovery of important organ functions such as liver function, heart function, kidney function and blood coagulation function, which can greatly reduce mortality, reduce the number of hospitalized days of cured patients, and be able to alleviate the pressure on medical resources.

LIMITATIONS OF THE STUDY

The study was carried out in one department of the hospital. The authors intend to not only expand it to the whole hospital but also make it multi-center, if the resources (financial and others) are available.

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CONFLICT OF INTEREST

None to declare.

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None to disclose.

REFERENCES

1. WHO. Coronavirus disease. 2019 (COVID-19): situation report-204. 2020. Available online at https://www.who.int/emergencies/diseases/novel-coronavirus2019/situation-reports). [Last accessed August 14 2020].
2. Wu Z, McGoogan JM. Characteristics of and important lessons from the Coronavirus Disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 cases from the Chinese center for disease control and prevention. JAMA. 2020; 323 (13): 1239–42.
3. Du RH, Liang LR, Yang CQ, Wang W, Cao TZ, Li M, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. Eur Respir J. 2020; 55 (5): 2000524-7.
4. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A trial of Lopinavir-Ritonavir in adults hospitalized with severe COVID-19. N Engl J Med. 2020; 382 (19): 1787-99.
5. National Health Commission of the People's Republic of China. 2020. Issuing the new coronavirus pneumonia diagnosis and treatment plan (Trial Version 7). Available online at: http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml. [Last accessed on October 19th , 2020].
6. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol Hepatol. 2020; 5 (5): 428-30.
7. Li J, Fan JG. Characteristics and mechanism of liver injury in 2019 Coronavirus Disease. J Clin Transl Hepatol. 2020; 8 (1): 13-7.
8. Li T, Lu H, Zhang W. Clinical observation and management of COVID-19 patients. Emerg Microbes Infect. 2020; 9 (1): 687-90.
9. Zhao Y, Zhao Z, Wang Y, Zhou Y, Ma Y, Zuo W. Single-cell RNA expression profiling of ACE2, the receptor of SARS-CoV-2. Am J Respir Crit Care Med. 2020; 202 (5): 756-9.
10. D'Ardes D, Boccatonda A, Rossi I, Guagnano MT, Santilli F, Cipollone F, et al. COVID-19 and RAS: Unravelling an unclear relationship. Int J Mol Sci. 2020; 21 (8): 3003-9.
11. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol. 2020; 5 (7): 802-10.
12. Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol. 2020; 109 (5): 531-8. [Epub ahead of print].
13. Hendren NS, Drazner MH, Bozkurt B, Cooper LT. Description and proposed management of the acute COVID-19 cardiovascular syndrome. Circulation. 2020; 141 (43): 1903-14.
14. Angel-Korman A, Brosh T, Glick K, Leiba A. [COVID-19, the kidney and hypertension]. Harefuah. 2020; 159 (4): 231-4.
15. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020; 97 (5): 829-38. [Epub ahead of print].
16. Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. Acta Diabetol. 2010; 47 (3): 193-9.
17. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes Metab Syndr. 2020; 14 (4): 303-10.
18. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev. 2020; 2 (1): 1-9. [Epub ahead of print].
19. Ma WX, Ran XW. The management of blood glucose should be emphasized in the treatment of COVID-19. Sichuan Da Xue Xue Bao Yi Xue Ban. 2020; 51 (2): 146-50.

Author's Contribution

ZL: Conception and acquisition of data, drafting of the work.

JL: Acquisition of data, drafting of the work.

ALL AUTHORS: Approval of the final version of the manuscript to be published.