

Association between the Level of HbA1C and Prognosis of COVID-19 in Diabetic Patients

Malick Maria Alvi*, Abdul Samad, Sara Ahmed, Ahsan Ali Gaad and Eraj Aman

Department of Medicine, Patel Hospital, Karachi, Pakistan

Abstract

Objective: To determine the association between the HbA1C level and prognosis of COVID-19 in diabetic patients.

Abstract: SARS-CoV has emerged as a major economical and health crisis in the modern world. New strains and diverse clinical cases possess management challenges. As diabetes is found to be common comorbidity among the COVID infected individuals, our study focuses on the impact of diabetes control *i.e.* HbA1C levels on the outcome and severity of illness.

Methodology: This is a retrospective cohort study. Data were collected retrospectively from the registry. COVID patients with prediabetes, diabetes and newly diagnosed diabetes were included from April 2020 to March 2021, in the COVID units of Patel hospital Karachi, Pakistan. Asymptomatic stages of COVID-19 were excluded from the study. Study participants were included in the survey by purposive sampling. All the patients diagnosed with COVID-19 were recorded for demographic data, past medical history, history of comorbid conditions, symptoms, laboratory random blood sugars, HbA1C levels, radiological findings and outcomes. The control of diabetes was compared with the severity of symptoms, clinical stage of disease, oxygen demand, and also the outcome of the disease in terms of hospital stay and mortality.

Results: 82 COVID patients with previous or newly diagnosed diabetes were included in the study. Mean age was 61 years, 71% (n=58) were male, 29% (n=24) were female. 73% (n=60) were diagnosed cases of diabetes, while 26.83% (n=22) were newly diagnosed diabetes. On comparing HbA1C levels with age and gender no significant relationship was found but smoking and diabetes without end organ damage was significantly related to the worsening HbA1c *i.e.* uncontrolled diabetes. Comparison of HbA1C levels with severity of illness showed that most patients 63.2% (n=36) with the severe stage of COVID-19 were having uncontrol HbA1C levels *i.e.* HbA1C >7.5%. 63% (n=44) had respiratory failure depicting a higher ratio of respiratory failure in the uncontrolled HbA1C group. However HbA1C levels were not found to have a significant effect on mortality. HbA1c levels do not have an impact on the length of stay of patients but significant correlation with PFR *i.e.* PaO₂ and FIO₂ ratio which is a marker of respiratory failure.

Conclusion: As diabetic patients who contracted COVID-19 infection are more prone to get severe illness, this signifies the importance of diabetes control as one of the key management and safety strategy for COVID-19 infection. However, it has little impact on mortality.

Keywords: COVID-19; HbA1C; Radiological findings; Prognosis; Diabetes

Introduction

SARS-CoV-2 pandemic poses significant health, economic and financial crises all over the globe [1,2]. As the SARS-CoV-2 pandemic is accelerating, its new dimensions are being discovered. As diabetes is one of the leading comorbidity around the world, SARS-CoV-2 effects on the diabetic patient is an area of research to be discovered. Many studies have revealed the fact that clinical course and outcomes of COVID-19 infection are affected by aging and comorbidities *i.e.* a higher ratio of disease severity and an increased mortality rate was found in patients with ischemic heart disease, diabetes mellitus and hypertension [3,4].

The incidence of diabetes in patients with COVID-19 was estimated to range from 5% to 20% in some studies similarly, the prevalence of diabetes was reported at 28.3% in hospitalized patients in the USA in the COVID-19 associated hospitalization surveillance network (COVID-NET) [5].

A comparative study conducted in China showed that diabetic patients with COVID-19 infection were more likely to fall into

*Corresponding author: Malick Maria Alvi, Department of Medicine, Patel Hospital, Karachi, Pakistan, Tel: 923363230240; E-mail: dr.mariamalick@gmail.com

Received: 11-December-2022, Manuscript No. JIDT-22-83089; **Editor assigned:** 13-December-2022, PreQC No. JIDT-22-83089 (PQ); **Reviewed:** 27-December-2022, QC No. JIDT-22-83089; **Revised:** 24-March-2023, Manuscript No. JIDT-22-83089 (R); **Published:** 31-March-2023, DOI: 10.4172/2332-0877.1000545

Citation: Alvi MM, Samad A, Ahmed S, Gaad AA, Aman E (2023) Association between the Level of HbA1C and Prognosis of COVID-19 in Diabetic Patients. J Infect Dis Ther 11: 545.

Copyright: © 2023 Alvi MM, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

critical illness with complications and a high mortality rate [6]. Similarly, other studies and data also depict the relationship between the poor glycemic control and worsening outcome of COVID-19 infection [7,8].

It is proposed that long term suboptimal glycemic control may impair several aspects of the immune response to viral infection and high levels of inflammatory markers are present in diabetic patients contributing to the severity of COVID-19 infection and hypercoagulability which contribute to the worse outcomes of disease [9,10].

In Pakistan, the SARS-CoV-2 outbreak has affected approximately 1.5 million individuals with thousands being dead. Pakistan is also a country where the prevalence of diabetes is estimated to be high. However, the local data on the effect of glycemic control on the severity of COVID-19 infection is lacking. To our knowledge, our study is unique in analyzing the impact of diabetes control on the severity and outcome of COVID-19. This study will also include patients with newly diagnosed diabetes, whereas most studies across the world are conducted on already diagnosed diabetic patients.

Materials and Methods

This is a retrospective cohort study. Data were collected retrospectively from the registry. Study participants were diabetic patients (already diagnosed and newly diagnosed), prediabetes, diabetes mellitus type 1 and diabetes mellitus type 2, admitted with COVID-19 infection, from April 2020 to March 2021. The study was conducted in COVID units of Patel hospital Karachi, Pakistan. Study participants were included in the survey by purposive sampling. Patients with the asymptomatic stage of COVID-19 were excluded from the study.

All the diabetic and prediabetic patients admitted to the COVID unit of Patel hospital were analyzed for the severity of the disease as determined by the clinical stage of the disease, cytokine release storm, hypoxia and its correlation with their diabetes control was studied and also impact of HbA1C levels *i.e.* diabetes control on the outcome of the disease was studied.

Data collection was carried out by standardized questionnaire. All the patients diagnosed with COVID-19 were recorded for demographic data, past medical history, history of comorbid conditions, symptoms, signs *i.e.* respiratory rate and hypoxia and laboratory results (neutrophil count, procalcitonin, percentage of lymphocyte, neutrophil lymphocytes ratio, ECG, trop I, D-dimers, C-reactive protein and serum ferritin), random blood sugars, HbA1C levels, radiological findings. Treatment modalities (*i.e.* antiviral therapy, oxygen and supportive respiratory therapy, corticosteroid therapy, renal replacement therapy and other supportive care were also recorded. Also, the outcomes of disease were documented in the form of improved and discharged or worsened and expired.

Patients were categorized into mild, moderate and severe or critical stages of illness according to their clinical history and examination findings which are respiratory rate, oxygen saturation in room air and radiological findings *i.e.* chest X-ray findings, levels of inflammatory markers, and multi-organ involvement. Control of diabetes was assessed by HbA1C taken within 3 months or on admission or during the course of illness. Values of more than 7.5% were labeled as uncontrolled. Antidiabetic medication oral drugs or insulin, duration

of diabetes, drug compliance and other comorbid conditions were also recorded.

Different treatment modalities in the hospital for COVID-19 infection *i.e.* antibiotics, oxygen support, invasive or noninvasive ventilation, steroids, antivirals, and anti-cytokine release syndrome medication *i.e.* anti-interleukin 6 antibodies medication or steroids or convalescent plasma were also documented.

The control of diabetes was compared with the severity of symptoms, clinical stage of disease, oxygen demand and also the outcome of the disease in terms of mortality and hospital stay.

Operational definitions

Diabetes mellitus: A random plasma glucose ≥ 200 mg/dl (11.1 mmol/l, in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis or HbA1C is more than or equal to 6.5%.

Prediabetes: It is defined as fasting blood glucose between 100 mg/dl to 126 mg/dl or HbA1C level between 5.7% to 6.4%.

COVID-19 cases: Patients presenting with symptoms suggestive of COVID-19 (*i.e.* fever, cough, sore throat, shortness of breath, nausea, vomiting, diarrhea, irritability or loss of smell or taste) along with laboratory test positive for the COVID-19 from the nasopharyngeal specimen by the real time Reverse Transcription-Polymerase Chain Reaction (RT-PCR) assay within last four weeks or positive serology.

Clinical stages

COVID-19 patients can be categorized according to the different stages of illness.

Mild illness: Patients with one or more of the listed signs and symptoms (e.g., fever, cough, sore throat, headache, myalgia, malaise) without shortness of breath or chest X-ray findings with normal oxygen saturation on room air.

Moderate illness: Patients who experience symptoms, a respiratory rate less than 30, consolidation or other findings on chest imaging <50%, having oxygen saturation between 90%-93% on room air.

Severe illness: Patients having respiratory rate >30 breaths per minute, SpO₂ <90% on room air or lung infiltrates >50% on chest X-ray.

Critical illness: Patients who show advanced symptoms, developed acute respiratory distress syndrome, septic shock, acute kidney injury or multiorgan dysfunction falls in this category.

Outcomes: Outcomes will be defined in terms of length of hospital stay, respiratory failure, duration of mechanical ventilation, the complication of disease *i.e.* Acute Respiratory Distress Syndrome (ARDS), acute renal failure, cardiac dysfunction, thromboembolic complications, septic shock, stroke and mortality during the hospital stay and clinical recovery.

Respiratory failure: Respiratory failure is defined as arterial oxygen PaO₂ <60 mmHg.

Acute Respiratory Distress Syndrome (ARDS): According to Berlins' definition, acute respiratory distress syndrome is acute hypoxic respiratory failure in the period of one week with normal cardiac function and accompanied by a chest X-ray showing bilateral infiltrates. Hypoxemic respiratory failure is divided according to different values of PaO₂/FiO₂.

- PaO₂/FiO₂ ratio between 200 to 300.
- PaO₂/FiO₂ ratio between 100 to 200.
- PaO₂ and FiO₂ ratio less than 100.

Acute kidney injury: It is defined by the Acute Kidney Injury Network (AKIN) criteria *i.e.* a rise in serum creatinine \geq 0.3 mg/dl from the baseline or an increase in serum creatinine 1.5 times from the normal baseline in a period of 48 hours.

Cardiac dysfunction: The cardiac injury will be defined as the elevated serum levels of troponin I with ECG changes.

Thromboembolic complication: Elevated D-dimer levels with pulmonary embolism proved on CT pulmonary angiogram, stroke with CT/MRI brain changes or myocardial infarction documented on ECG changes and troponin levels/echocardiographic findings.

Septic shock: It is defined as persistent hypotension despite volume resuscitation, requiring vasopressors to maintain MAP \geq 65 mmHg.

Cytokine release syndrome: It is characterized by the dysregulated host immune response to the COVID-19 infection due to the activation of macrophages and lymphocytes. The following parameters can be used to predict the cytokine release syndrome:

- Ferritin >1000 mcg/L and rising in last 24 hrs.
- B-Ferritin >2000 in patients with high oxygen demand.
- Lymphopenia <20%.

Neutrophil Lymphocyte Ratio (NLR) >5 and 2 of the following:

- CRP >70 mg/l and rising trend.
- LDH >300 Iu an rising trend.
- D-Dimer >1000 ng/ml (1 mcg/ml) and rising trend.
- Ferritin >700 mcg/ml and rising trend.

Statistical analysis

SPSS version 21 was used to analyze the data. Shapiro Wilk test was performed to test the normality of distribution for all continuous variables such as age, length of stay, oxygen demand, PFR and FiO₂. Variables that were found to be normal were presented with average and standard deviation while variables that were not found to be normal were reported by median and interquartile range. Mann Whitney U test was performed to compare the mean for all non-parametric continuous variables *i.e.* oxygen demand, PFR, FiO₂ and length of stay. All qualitative variables like gender, COVID antibody, Charlson index, comorbid, and the severity of COVID-19 were presented in terms of counts and percentages. The association of HbA1c with basic demographic of the patient like age, gender,

smoking habit and diabetes without end organ damage was examined by performing a *chi-square* or Fisher exact test.

The impact of HbA1c was examined on many variables like the severity of COVID-19, complications and symptoms by using the *chi-square* or Fisher exact test, mean comparison was done for oxygen demand, PFR, FiO₂ and length of stay by performing the Mann-Whitney U test.

Results

82 COVID patients who were diabetics or newly diagnosed diabetics were included in the study. Mean age was 61 years, 71% (n=58) were male, 29% (n=24) were female, 33% (n=27) were hypertensive which is the most common comorbidity in COVID patients. 73% (n=60) were diagnosed cases of diabetes, while 26.83% (n=22) were newly diagnosed diabetes. 57% (n=47) patients presented with severe stage of COVID and their oxygen demand was high, followed by moderate illness 26% (n=21), 11% were smoker, fever was the most common presenting complain *i.e.* 87% (n=71) followed by cough 74%, shortness of breath 72% (n=59) and generalized weakness 22% (n=18). Cytokine release syndrome was the most common complication of the disease *i.e.* 82% (n=67) followed by acute kidney injury 20% (n=16). On comparing HbA1C levels with age and gender there were no significant results but smoking was significantly related to the worsening HbA1C *i.e.* uncontrolled diabetes. It indicates a strong impact of smoking cessation on the control of diabetes.

Most patients 63.2% (n=36) with a severe stage of COVID-19 were found to have uncontrolled HbA1C levels *i.e.* HbA1C >7.5% but it is not statistically significant (p-value=0.829). 63% (n=44) of participants had a respiratory failure in uncontrolled diabetes group in comparison to the well-controlled diabetes group where 36.2% (n=25) had respiratory failure depicting a higher ratio of respiratory failure in the uncontrolled HbA1C group however the relation of uncontrolled diabetes with the higher ratio of respiratory failure was not significant (p-value=0.232). Similarly, CRS was found more in the uncontrolled HbA1C group *i.e.* 59% (n=40). 70.8% (n=17) dead patients were found to have uncontrolled diabetes however, HbA1C levels were not found to have a significant effect on mortality (p-value=0.239) (Tables 1 and 2). Out of 14 patients who required mechanical ventilation 10 were having uncontrolled diabetes *i.e.* 71%. HbA1c levels do not have a significant impact on the length of stay of patients but significant

correlation with worsening PFR *i.e.* PaO₂ and FiO₂ ratio which is a marker of respiratory failure *i.e.* mean PFR was (76.5 \pm 84.14) in uncontrolled diabetes or raised HbA1C levels group while PFR is (110.5 \pm 208.50) in controlled HbA1c group (Table 3).

Demographics		
Variable	Frequency (%)	
Gender	Male	58 (71%)
	Female	24 (29%)
Age in years	Mean \pm S.D	
	61 \pm 13	
Length of stay in days	Median \pm IQR	

	6 ± 5	
COVID antibody	IgM positive and IgG negative	14 (17%)
	IgM negative and IgG positive	6 (7%)
	Both positive	16 (20%)
	Both negative	10 (12%)
Comorbid	Hypertension	27 (33%)
	Myocardial infarction	15 (18%)
	Congestive heart failure	1 (1%)
	Cerebrovascular disease	3 (4%)
	Chronic pulmonary disease	5 (6%)
	Peptic ulcer disease	1 (1%)
	Diabetes without end organ damage	49 (60%)
	Hemiplegia	1 (1%)
	Moderate or severe renal disease	1 (1%)
	Diabetes with end organ damage	10 (12%)
	Metastatic solid tumor	1 (1%)
	AIDS (not just HIV positive)	1 (1%)
Severity on presentation	Mild	7 (9%)
	Moderate	21 (26%)
	Severe	47 (57%)
Complications	Stroke	1 (1%)
	Acute kidney injury	16 (20%)
	Cytokine release syndrome	67 (82%)
Smoking		9 (11%)
Symptoms	Fever	71 (87%)
	Cough	61 (74%)
	Sore throat	6 (7%)
	Runny nose	1 (1%)
	Body aches	1 (1%)
	Generalized weakness	18 (22%)
	Irritability confusion	4 (5%)
	Shortness of breath	59 (72%)
	Diarrhea	13 (16%)
	Vomiting	4 (5%)
	Ageusia (loss of taste)	2 (2%)
DM diagnosis	Old	60 (73.17%)

	New	22 (26.83%)
DM type	Type 1 diabetic	0 (0.0%)
	Type 2 diabetic	82 (100%)
DM without end organ	Yes	49 (59.8%)
	No	33 (40.2%)

Table 1: Comparison of HbA1C levels with demographics, course and outcome of COVID-19 infection.

Variable		HbA1C (output)		P-value
		Controlled (n, %)	Uncontrolled (n, %)	
Age	≤ 35	1 (33.3%)	2 (66.7%)	0.320 F
	36-55	3 (12.0%)	22 (88.0%)	
	>55	13 (24.1%)	41 (75.9%)	
Gender	Male	10 (17.2%)	48 (82.8%)	0.243 F
	Female	7 (29.2%)	17 (70.8%)	
Diabetes without end organ damage	No	14 (42.4%)	19 (57.6%)	<0.001
	Yes	3 (6.1%)	46 (93.9%)	
Smoking	No	13 (17.8%)	60 (82.2%)	0.083 F
	Yes	4 (44.4%)	5 (55.6%)	

Table 2: Variable frequency (%).

Variable		HbA1C		P-value
		Controlled (n, %)	Uncontrolled (n, %)	
Severity of COVID-19				
Mild		4 (44.4%)	5 (55.6%)	0.829
Moderate		7 (43.8%)	9 (56.3%)	
Severe		21 (36.8%)	36 (63.2%)	
Complications				
Myocardial infarction		7 (46.7%)	8 (53.3%)	0.502
Stroke		0 (0.0%)	1 (100.0%)	0.999
Respiratory failure		25 (36.2%)	44 (63.8%)	0.232
Acute kidney injury		7 (43.8%)	9 (56.3%)	0.666
Hemodialysis		0 (0.0%)	1 (100.0%)	0.999
Cytokine release syndrome		27 (40.3%)	40 (59.7%)	0.617
Discharge status	Alive	25 (43.1%)	33 (56.9%)	0.239

	Dead	7 (29.2%)	17 (70.8%)	
Symptoms				
Fever		28 (39.4%)	43 (60.6%)	0.999
Cough		21 (34.4%)	40 (65.6%)	0.146
Shortness of breath		19 (32.2%)	40 (67.8%)	0.043
Need for ventilator		4 (28.6%)	10 (71.4%)	0.379
Oxygen demand	Median ± IQR	(15.0 ± 12.75)	(15.0 ± 15.0)	0.566
PFR	Median ± IQR	(110.5 ± 208.50)	(76.5 ± 84.14)	0.003
FiO ₂	Median ± IQR	(72.5 ± 52)	(80.0 ± 45.0)	0.153
Length of stay	Median ± IQR	(5.50 ± 6)	(6.50 ± 5.0)	0.176

Table 3: Outcome of COVID-19 infection.

Discussion

COVID-19 has emerged as a big humanitarian crisis which affected the whole world. It shows a sudden surge of cases along with increased mortality. New waves of infection keep erupting in various parts of the world with a more strong and resistant strain of the virus. Different research in this area highlights the relation between immunocompromised status and severity of illness. In Pakistan diabetes is one of the prevalent illnesses and a large number of diabetic patients have been affected by this pandemic so our study focused on the association between the HbA1C levels *i.e.* diabetes control and prognosis of COVID-19 in terms of mortality, oxygen demand and hospital stay. In our study majority were male 71% and 29% female, while C-Gebhard and Qian J, et al., and others studied that there is less disparity between both gender in terms of attack rate or contracting illness but mortality and severity of illness are found more in males as compared to female, however, infection rates among gender can differ due to difference in the demographics [11-15]. The mean age of admitted patients was 61 years. As described according to the CDC that rate of hospitalization among people of age 50 years to 64 years is 4 times higher and among those aged 65 to 74 is 5 times higher as compared to the younger COVID patients [16]. 73% of patients were diagnosed cases of diabetes while 26.8% of patients were newly diagnosed with diabetes compared to the results in Smith SM, et al., which showed 62% of patients with diabetes highlighting the fact that diabetes plays a contributory role in the onset of illness and also one of the most common comorbidity among COVID infected patients [17]. In our study fever 87%, cough 74% and shortness of breath 72% were the most frequently observed symptoms comparable to results shown in different studies where fever and cough are the most common symptoms in COVID patients followed by dyspnea [18,19].

63% of COVID patient with uncontrolled diabetes was associated with severe and critical COVID while 36% of COVID patients with controlled diabetes were associated with a severe stage of COVID. This also signifies the relation of diabetes with the severity of illness. Smith and Wang Z, et al., and several others also support this which impaired glycemic control is associated with worsening of disease. In our study cytokine release syndrome is defined as activation of the immune system against the COVID virus and increased inflammatory response of the body suggested by increased

ferritin, LDH and CRP. This study demonstrated that the most common complication of the disease was cytokine release syndrome followed by acute kidney injury. Although 59% of patients with uncontrolled HbA1C levels >7.5% were having cytokine release syndrome in comparison to 40% of patients in the controlled HbA1C group values of HbA1C levels are not significantly related to the cytokine release syndrome, against the results of the study conducted in China showed a significant relationship between the cytokine release syndrome and worsening HbA1C levels [20].

53% of patients in the uncontrolled HbA1C group were having acute kidney injury as compared to 46% in the controlled group which depicts that worsening diabetes can have strong impact in the manifestation of complication of COVID-19.

It is observed in this study that compared to the controlled HbA1C group, uncontrolled diabetes group were more affected with respiratory failure, which signifies the importance of good glycemic control in overall prognosis and outcome of this infection. Zhu Z and Rysz S, et al., also highlights the significant increase ratio of respiratory failure in poorly controlled diabetes mellitus [21].

Patients in the uncontrolled HbA1C group were presented with shortness of breath more as compared to those without the controlled HbA1C group. 67.2% of patients presented with shortness of breath were found to have uncontrolled HbA1C, which confirms that uncontrolled diabetes was associated with more symptomatic shortness of breath, similar findings of increased and severe symptoms of COVID-19 were reported in patients with uncontrolled diabetes in the study conducted in India. Similarly, PaO₂ and FiO₂ ratio *i.e.* the ratio of partial pressure of oxygen in blood and the fraction of inspired oxygen which is a marker of the severity of respiratory failure was significantly related to the HbA1C levels *i.e.* uncontrolled diabetes was more prone to respiratory failure.

However, in contrast to other studies, our study does not find any significant correlation between the uncontrol HbA1C with mortality. Although 70% of patients who died had uncontrolled diabetes but the results were not significantly correlated with mortality, against the result found in other studies while comparable to the result found in a study conducted in the UK which revealed no significant difference in mortality and complication among diabetes control and uncontrolled group. The disparity in affecting mortality rate in the uncontrol

diabetes group might be due to different populations and small sample sizes.

Correlation of smoking with HbA1C was found to be positive *i.e.* smokers had uncontrolled HbA1C as compared to nonsmokers, which showed that smoking is a contributory factor to insulin resistance. However, a study conducted in Indonesia showed that smoking has a worse impact on post-prandial glucose levels while having no impact on HbA1c levels and fasting glucose levels.

The limitation of our study is small sample size and single centered study so results cannot be generalized. One of the main strength of study is that it finds some new dimension of the COVID-19 with diabetes and number of researches related to study the association between diabetes and COVID-19 in terms of clinical course and prognosis of the disease is limited so our work will add valuable information to this subject.

Conclusion

This study signifies the importance of glycemic control *i.e.* HbA1C level on the course of COVID-19 illness and management of disease in diabetic and newly diagnosed diabetic patients. HbA1C could be a good marker for predicting the severity of COVID-19 infections and will help the clinician to use it as a tool for risk stratification in the future so that high risk groups could be prevented by vaccination and adequately managed.

Funding

The author did not receive support from any organization for the submitted work.

Conflict of Interest/Competing Interest

The authors have no conflict of interest to declare that are relevant to the content of the article.

References

1. She J, Jiang J, Ye L, Hu L, Bai C, et al. (2020) Novel coronavirus of pneumonia in Wuhan, China: Emerging attack and management strategies. Clin Transl Med 9: 19.
2. Yang J, Zheng Y, Gou X, Pu K, Chen Z, et al. (2020) Prevalence of comorbidities in the novel Wuhan Coronavirus (COVID-19) infection: A systematic review and meta-analysis. Int J Infect Dis 94: 91-95.
3. Zhou F, Yu T, Du R, Fan G, Liu Y, et al. (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet 395: 1054-1062.
4. Garg S (2020) Hospitalization rates and characteristics of patients hospitalized with laboratory confirmed Coronavirus disease 2019 COVID-NET, 14 states. MMWR Morb Mortal Wkly Rep 69.
5. Zhang Y, Cui Y, Shen M, Zhang J, Liu B, et al. (2020) Association of diabetes mellitus with disease severity and prognosis in COVID-19: A retrospective cohort study. Diabetes Res Clin Pract 165: 108227.
6. Wu J, Huang J, Zhu G, Wang Q, Lv Q, et al. (2020) Elevation of blood glucose level predicts worse outcomes in hospitalized patients with COVID-19: A retrospective cohort study. BMJ Open Diabetes Res Care 8: e001476.
7. Hussain A, Bhowmik B, Moreira DVNC (2020) COVID-19 and diabetes: Knowledge in progress. Diabetes Res Clin Pract 162: 108142.
8. Wang Z, Du Z, Zhu F (2020) Glycosylated hemoglobin is associated with systemic inflammation, hypercoagulability and prognosis of COVID-19 patients. Diabetes Res Clin Pract 164: 108214.
9. Gebhard C, Regitz-Zagrosek V, Neuhauser HK, Morgan R, Klein SL (2020) Impact of sex and gender on COVID-19 outcomes in Europe. Biol Sex Differ 11: 29.
10. Qian J, Zhao L, Ye RZ, Li XJ, Liu YL (2020) Age dependent gender differences in COVID-19 in mainland China: Comparative study. Clin Infect Dis 71: 2488-2494.
11. Smith SM, Boppa A, Traupman JA, Unson E, Maddock DA, et al. (2021) Impaired glucose metabolism in patients with diabetes, prediabetes and obesity is associated with severe COVID-19. J Med Virol 93: 409-415.
12. Chen Y, Yang D, Cheng B, Chen J, Peng A, et al. (2020) Clinical characteristics and outcomes of patients with diabetes and COVID-19 in association with glucose lowering medication. Diabetes Care 43: 1399-1407.
13. Yuan S, Li H, Chen C, Wang F, Wang DW (2021) Association of glycosylated haemoglobin HbA1C levels with outcome in patients with COVID-19: A retrospective study. J Cell Mol Med 25: 3484-3497.
14. Zhu Z, Mao Y, Chen G (2021) Predictive value of HbA1c for in-hospital adverse prognosis in COVID-19: A systematic review and meta-analysis. Prim Care Diabetes 15: 910-917.
15. Rysz S, Fagerlund MJ, Rimes-Stigare C, Larsson E, Jalde FC, et al. (2022) Chronic dysglycemia and risk of SARS-CoV-2 associated respiratory failure in hospitalized patients. Acta Anaesthesiol Scand 66: 48-55.
16. Bhandari S, Rankawat G, Singh A, Gupta V, Kakkar S (2020) Impact of glycemic control in diabetes mellitus on management of COVID-19 infection. International J Diabetes Dev Ctries 40: 340-345.
17. Prattichizzo F, de Candia P, Nicolucci A, Ceriello A (2021) Elevated HbA1c levels in pre COVID-19 infection increases the risk of mortality: A systematic review and meta-analysis. Diabetes Metab Res Rev 38: e3476.
18. Alkundi A, Mahmoud I, Musa A, Naveed S, Alshawwaf M (2020) Clinical characteristics and outcomes of COVID-19 hospitalized patients with diabetes in the United Kingdom: A retrospective single centre study. Diabetes Res Clin Pract 165: 108263.
19. Patel AJ, Klek SP, Peragallo-Dittko V, Goldstein M, Burdge E, et al. (2021) Correlation of hemoglobin A1C and outcomes in patients hospitalized with COVID-19. Endocr Pract 27: 1046-1051.
20. Randhawa G, Syed KA, Singh K, Kundal SV, Oli S, et al. (2021) The relationship between obesity, hemoglobin A1C and the severity of COVID-19 at an urban tertiary care center in New York city: A retrospective cohort study. BMJ Open 11: e044526.
21. Sari MI, Sari N, Darlan DM, Prasetya RJ (2018) Cigarette smoking and hyperglycaemia in diabetic patients. Open Access Maced J Med Sci 6: 634-637.