ejpmr, 2021,8(1), 48-54

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article
ISSN 2394-3211
EJPMR

THE EFFECT OF DIABETES LEVEL OF CONTORL ON COVID-19 SEVERITY AND MORTALITY: A RETROSPECTIVE COHORT STUDY

Dr. Nada Bassam Rabie[1]*, Dr. Muneera Abdulmalik Alshareef[2], Dr. Samia Abdullah Bokhari[3], Dr. Abdullah M. Mallisho[2], Dr. Turki Abdulaziz Alharthi[2], Dr. Ghada Asim Rayes[4], Dr. Waleed Omar Bawazeer[5], Dr. Rehab Mahmoud Elboraie[6], Dr. Ameera Husseian Alzahrani[5], Dr. Hamdy Abdelwareth Alkady[6], Dr. Mohamed Sayed Galal[6] and Hanin Abdulhameed Shalaby[7]

[1]Consultant (Infectious Disease), King Fahd Armed Forces Hospital, Jeddah – Saudi Arabia.
[2]Consultant (Endocrine), King Fahd Armed Forces Hospital, Jeddah – Saudi Arabia.
[3]Consultant and Head of Department (Endocrine), King Fahd Armed Forces Hospital, Jeddah – Saudi Arabia.
[4]Consultant (Family Medicine), King Fahd Armed Forces Hospital, Jeddah – Saudi Arabia.
[5]Fellow (Endocrine), King Fahd Armed Forces Hospital, Jeddah – Saudi Arabia.
[6]Specialist (Endocrine), King Fahd Armed Forces Hospital, Jeddah – Saudi Arabia.
[7]Specialist (Clinical Research and Data Management), King Fahd Armed Forces Hospital, Jeddah – Saudi Arabia.

***Corresponding Author: Dr. Nada Bassam Rabie**
Consultant (Infectious Disease), King Fahd Armed Forces Hospital, Jeddah – Saudi Arabia.

Article Received on 03/11/2020 **Article Revised on 23/11/2020** **Article Accepted on 13/12/2020**

ABSTRACT

Introduction: Since the beginning of COVID-19 pandemic, diabetes has been recognized to have important impact on the overall disease outcomes, including mortality. Exactly how this effect can vary according to the level of diabetes control is still unclear. **Method:** We conducted a retrospective cohort study to examine the association between disease outcome in terms of COVID-19 severity and mortality and the level of diabetes control. We collected data on baseline characteristics, HbA1C level, the total basal and bolus insulin and any previous documented complication such as diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemia (HHS). We compared the diabetes control before and after COVID infection. **Results:** 154 patients were included in our study. Mean age was 59.85 and 56% were males. Even in patients with Good/Fair diabetes control (HbA1C <8%), more than half presented with moderate CVOID-19 severity. Fasting blood sugar was elevated in 66%. While none developed HHS, 2% developed DKA. The mean length of hospital stay was 8 days. Even though mortality rate didn't vary across various levels of diabetes control, the need of insulin infusion was more in non-survivors (33% vs 4% in survivors, p-value 0.04). **Conclusion:** Our study clearly demonstrates that diabetes among hospitalized patients with COVID-19 puts them at higher risk of morbidity and mortality. This was especially associated with uncontrolled fasting hyperglycemia (>7mmol/L). Effective measures such as implementation of hyperglycemia algorithm for hospitalized patients and follow up plan should be implemented.

KEYWORDS: COVID-19, diabetes mellitus control, SARS-CoV-2, COVID-19 severity.

INTRODUCTION

Globally COVID-19 caused over half-million deaths by mid-2020. The majority of fatal cases were associated with chronic comorbidities.[1,2] Of those, diabetes was commonly reported, affecting between 9.7% to 33.8% of COVID-19 patients.[3,4] The impact of diabetes alone on the overall mortality rate is still evolving.[5–7]

Diabetes results in several metabolic alterations affecting the immune system.[8] Patients with diabetes are more prone to multiple bacterial infections, including abscesses and candidiasis.[9] The effect of diabetes on cell-mediated immunity and the risk in viral infection is not fully understood. Previous studies have shown worse outcome in diabetic patient affected with two closely-related viruses causing SARS and MERS-CoV.[10–12] Moreover, it's increasingly recognized that diabetes is rather a heterogenous disease, encompassing a wide spectrum of manifestations and various disease outcomes. Exactly how different levels of diabetes control affect the outcome of COIVD-19 patients remains unclear.

In this study, we aim to investigate the effect of diabetes control- as reflected by HbA1C level- on the severity and outcome of COVID-19 illness, including the need for ICU admission and mortality rate. At the same time, we want to examine the effect of COVID-19 on the post-discharge glycemic control.

METHODOLOGY

This study is a retrospective cohort study. All cases of confirmed COVID-19 infection evaluated in King Fahad Armed Forces Hospital in Jeddah-Saudi Arabia between April and June 2020 were assessed for eligibility. Patients are considered eligible if they are (1) 18 years old or above, (2) have confirmed COVID-19 infection in terms of positive PR-PCR from nasopharyngeal swab and (3) known or newly diagnosed to have diabetes on bases of HbA1c or random blood sugar within three months of enrollment. We included both hospitalized and non-hospitalized patients.

Data were extracted into a pre-coded electronic data collection sheet. Baseline characteristics included age, sex, pregnancy status, type of diabetes and the presence of other comorbidities. Diabetes control was assessed on bases of the most recent HbA1C, within three months of enrollment. Other variables included random blood sugar and the presence of diabetes-related complications such as nephropathy, retinopathy, diabetic foot, diabetic ketoacidosis (DKA), hyperosmolar hyperglycemic state (HHS) or hypoglycemia. We recorded the diabetic medications and the total change in units of basal and bolus before and during COVID-19 infection. Medications that might affect the overall outcome of COVID-19 patients as hydroxychloroquine, azithromycin, antibiotics and ACE/ARB inhibitors were also recorded.

COVID-19 was classified into asymptomatic, mild symptoms (URTI or predominant GI symptoms), moderate (shortness of breath not requiring oxygen), sever (desaturation, requiring oxygen), critical (admitted to ICU, requiring invasive or non-invasive ventilation) in accordance with the most recent MOH guideline.[13]

We aim to risk stratify COVID-19 patients' outcome according to the level of diabetes control as measured by HbA1C%. According to HbA1C% level, diabetes was good/fairly controlled if HbA1c is <8%, poorly controlled 8-10% or very poorly controlled if >10%. Our primary objective is to estimate all-cause mortality in COVID-19 patients according to the level of diabetes control. Secondary objectives are (1) to assess the need for ICU admission according to the level of diabetes control, and [2] to explore the effect of COVID-19 severity on the level of diabetes control during hospitalization.

RESULTS

A sample of 154 COVID-19 patients with diabetes was collected. Demographic and baseline characteristics of the sample participants are summarized in (table 1). The mean (±SD) age was 59.85 ± 14.362 and 86 (56%) patients were male. Around 40% of study participants had good/fair glycemic control (HbA1c <8), 31% had poor glycemic control (HbA1c ≥ 8 but less than 10) and 25% ha very poor glycemic control (HbA1c ≥ 10). History of previous acute glycemic complications included DKA in 3% of our study population and HHS in 2%. Two-thirds presented with moderate symptoms of covid-19 infection (Table 1). During hospital stay, majority (66%) had higher fasting blood glucose, with mean average fasting blood glucose (mmol/l) 8.28 ± 2.92. Postprandial blood glucose was better controlled in most patients 69 (58%). While none developed HHS, 2% developed DKA (all with underlying type1 DM). Six-percent (6%) of the patients needed intravenous insulin infusion to control in hospital hyperglycemia (of which 37.5% were DKA and 62.5% sever uncontrolled hyperglycemia). The mean length of hospital stay was 8 days ± 7.47.

The relationship between level of diabetes control and COVID-19 disease severity was explored in Table 2. Severe COVID-19 was seen in 17% of patients with fairly/good glycemic control, 32% with poor control and 22% with very poor control (P=0.65). The overall mortality rate was 3.4% and didn't vary significantly across different levels of diabetes control p-values > 0.05). This was consistent when we examined the relation according to the baseline HbA1C level and according to both fasting and postprandial blood sugar measures during hospitalization (table 3).

We looked into different factors that could influence the mortality rate such as occurrence of DKA, HHS, insulin basal/bolus dose, insulin infusion use, The rate of 30-days readmission, level of diabetes control and presence of microalbuminuria/ macroalbuminuria. Among those variables, only insulin infusion was required more in non-survivors (33%) compared with survivors (4%, p-value 0.04).

One-way ANOVA was used to compare length of stay according to the level of diabetes control and COVID-19 severity. There was no significant association according to the level of diabetes control (p = 0.72). Expectedly, patients with more severe COVID-19 and those requiring ICU admission had longer hospital stay (p < 0.001). Relationship between COVID-19 severity and level of diabetes control during hospitalization was examined using cross-tabulation analysis and Fisher's exact test (Table 2). No significant association was found with all p-values > 0.05. Relationship between COVID-19 severity and use of ACE/ARB inhibitors was examined (Table 2). No significant association was found with all p-values > 0.05.

DISCUSSION

Since March 2020, COVID-19 was announced as a global pandemic. Data from several publications showed that covid-19 associated with comorbidities such as diabetes mellitus, hypertension, cardiovascular diseases and chronic lung disease had worse outcomes and prognosis.[14,15] In our study we observed that the majority of patients with diabetes were more likely to experience moderate covid-19 symptoms at presentation, even in those who are considered to achieve fair/good diabetes control (HbA1C <8).

The median length of stay in our study sample was 6 days (table 3). This was shorter than what was reported from previous studies (with median between 10 to 13 days).[16,17] It should be noted however, that at the time of conducting this study, the Saudi national policy was mandating admission for all COVID patients, regardless of symptoms. A trend towards longer hospital stay was seen in patients with more severe COVID-19 symptoms, including patients requiring ICU admission. This was consistent with previous findings.[18,19]

Covid-19 patients with worse glycemic control have a longer hospital stay, as indicated by several previous published studies.[19] We found that the mean LOS for patients with fair/good glycemic control was 7.37 ± 6.86 days compared with 8.14 ± 7.61 days for patients with very poor glycemic control (p-value of 0.72).

Hyperglycemia is a common problem in hospitalized patients especially in acute conditions and severe infections. In particular, hyperosmolar hyperglycemic state and diabetic ketoacidosis were associated with increased morbidity and mortality.[20,21] Three patients in our study (1.94%) presented with DKA. All of them had underlying type 1 DM. This was consistent with other studies where DKA was present in nearly 2% of all individuals admitted to the hospital with COVID-19 and was associated with high morbidity and mortality.[22] In contrast, none of our DKA patients died. Previous studies reporting HHS as less prevalent than other hyperglycemic complications.[23,24] This finding matched with our results where there was no case of HHS reported.

Fasting blood sugar was uncontrolled (>7mmol/L) in 75% in patients requiring ICU admission, compared with 56% of those with mild symptoms (p-value of 0.61). Previous studies identified fasting hyperglycemia as an independent predictor for 28-day mortality in COVID-19 patients, with a threefold increase for those with fasting blood sugar of ≥7mmol/L(11). This was consistent with our finding that 67 % of cases that ended with mortality had uncontrolled fasting blood sugar (≥7mmol/L). Given the small number of patients who died during our study period, further evaluation and follow up are needed to draw a conclusion regarding this association.

Interestingly, our study showed that diabetes control not only influences the immediate outcome of COVID-19 patients but also the long-term control does affect the outcome. This was evident since 92% of survivors had controlled blood sugar during the period of follow up compared with only 50% in non-survivors (p <0.001).

Most deaths occurred in the same hospital setting (83%) rather than in those requiring readmission (16%).

We couldn't appreciate significant change in the total number of insulin units used to control blood sugar at baseline and during COVID-19 illness (Table 1, 3)

To our knowledge no studies looked on the effect of diabetic microvascular complications on COVID-19 presentation. In our study, we didn't find any association between covid-19 mortality and pre-existing diabetic micro or macro albuminuria. Similarly, our study didn't find any association between ACEI/ARB and covid-19 mortality in diabetic patients. This relation was examined before with conflicting results.[25]

Our study is limited by its retrospective nature and the small sample size. Also as a relatively small number of patients died, analysis of factors that could have affected mortality is limited. However, the rate of missing or incomplete data was relatively low. Almost all patients have documented HbA1C within three months of enrollment, a point which was lacking in other studies.[25]

Table 1. Demographic characteristics of sample participants

Demographic characteristics and baseline medical characteristics	**Frequency (%) or Mean ± SD [range]**
Hospital admission	
Yes	138 (90%)
No	16(10%)
Gender	
Male	86 (56%)
Female	68 (44%)
Age, years	59.85 ± 14.362 [14 – 93]
Charlson comorbidity index (CCI)	3.37 ± 2.136 [0 – 10]
HbA1c*	8.687 ± 2.134 [4.9 – 13.9]
Level of diabetes control at baseline **	
Very poor control (HbA1c > 10)	39 (25%)
Poor control (HbA1c 8-10)	48 (31%)
Good/ Fair control (HbA1c <8)	62 (40%)
Urine Alb/Cr ratio classification	
Normal—less than 3 mg/mmol	64 (42%)
Microalbuminuria—3-30 mg/mmol	35(23%)

Macroalbuminuria—More than 30 mg/mmol	24 (16%)
Previous DKA (diabetic ketoacidosis)	4 (3%)
Previous HHS (hyperosmolar hyperglycemic state)	3 (2%)
Home basal insulin (mean total units± SD)	64 (42%) 31.453±17.021 [8-70]
Home bolus insulin (mean total units± SD)	52 (33%) 50.961±30.61 [12-172]
Use of ACE/ARB inhibitors	82 (53%)
COVID symptoms Asymptomatic Mild Moderate Severe ICU admission	 2 (1%) 40 (26%) 70 (46%) 32 (21%) 9 (6%)

** HbA1c refers to the most recent hemoglobin A1c level within three months of COVID-19*
*** Classification of diabetes control was made based on the HbA1c level*

Table 2: The relation between COVID-19 severity and diabetes control.

Diabetes control measures	COVID -19 severity					P-value
	Asymptomatic	Mild	Moderate	Sever	ICU admission	
Level of diabetes control by HbA1C						
Fair/Good(HbA1c ≤ 8%)	2%	23%	54%	17%	4%	p = 0.65
Poor (HbA1c 8-10)	0%	18%	41%	32%	9%	
Very Poor(HbA1c > 10)	3%	17%	53%	22%	6%	
Fasting blood sugar level						
Uncontrolled (> 7mmol/L)	0 (0%)	9 (56%)	41 (67%)	19 (70%)	3 (75%)	p = 0.61
Controlled (≤ 7 mmol/L)	1 (100%)	7 (44%)	20 (33%)	8 (30%)	1 (25%)	
Postprandial blood sugar level						
Uncontrolled (> 10 mmol/L)	0 (0%)	7 (32%)	28 (45%)	11 (42%)	4 (50%)	p = 0.79
Controlled (≤ 10 mmol/L)	1 (100%)	15 (68%)	34 (55%)	15 (58%)	4 (50%)	
Use of ACE/ARB inhibitors						
No	2 (100%)	19 (47.5%)	36 (52%)	9 (28%)	5 (56%)	p = 0.09
Yes	0 (0%)	21 (53%)	34 (49%)	23 (72%)	4 (44%)	

Table 3: Diabetes control during COVID-19

Hospital stay details	**Frequency (%) or Mean ± SD [range]**
Average fasting blood glucose (mmol/l)	8.28 ± 2.92 [4.4 – 22.0]
Fasting blood glucose level Uncontrolled (> 7 mmol/L) Controlled (≤ 7 mmol/L)	 73 (66%) 37 (34%)
Average postprandial blood glucose, (mmol/l)	10.07 ± 2.98 [4.9 – 20.0]
Postprandial blood glucose level Uncontrolled (> 10 mmol/L) Controlled (≤ 10 mmol/L)	 51 (42%) 69 (58%)
Hospital DKA	3 (2%)

Hospital HHS	0 (0%)
Hospital basal insulin (mean total units± SD)	77 (56%) 29.2±14.50395 [10-72]
Hospital bolus insulin (mean total units± SD)	62 (45%) 45.3594 ± 33.360 [5-172]
Hospital insulin infusion use	8 (6%)
Length of hospital stay,(days)	8 ± 7.47 [1 – 41] Median = 6

DKA=diabetic ketoacidosis, HHS= hyperosmolar hyperglycemic state

Table 4: Relationship between the COVID Mortality rate and some clinical factors.

Clinical factors	**COVID Mortality Frequency (%)**		**P-Value**
	Survived	**Dead**	
Hospital DKA Yes No	3 (2 %) 129 (98 %)	0 6 (100%)	0.71
Hospital Basal Insulin Yes No	73 (55 %) 59 (45 %)	4 (67 %) 2 (33 %)	0.58
Hospital Bolus Insulin Yes No	58 (44 %) 74 (56 %)	4 (67 %) 2 (33 %)	0.274
Hospital Insulin Infusion Use Yes No	6 (4 %) 125 (95 %)	2 (33 %) 4 (67 %)	0.040*
Post Discharge Diabetes Control Controlled Not Controlled	118 (92 %) 10 (8 %)	3 (50 %) 3 (50 %)	< 0.001**
30 Days Re-admission Re-Admitted Not-readmitted	9 (7 %) 122 (93 %)	1 (16 %) 5 (83 %)	0.13
Level of Diabetes control at Baseline Very poor control (HbA1c > 10) Poor control (HbA1c 8-10) Fairly control (HbA1c ≤ 8)	37 (29 %) 42 (33 %) 48 (38 %)	0 2 (33 %) 4 (67 %)	0.23
Fasting Blood Sugar level Uncontrolled > 7 Controlled ≤ 7	69 (66 %) 36 (34 %)	4 (67 %) 1 (33 %)	0.50
Postprandial Blood Sugar level Uncontrolled > 10 Controlled ≤ 10	48 (42 %) 66 (58 %)	3 (50 %) 3 (50 %)	0.70
Urine Alb Cr Ratio Normal > 3 Micro Albuminuria 3-30 Macro Albuminuria < 30	56 (53 %) 27 (26 %) 22 (21 %)	2 (40 %) 2 (40 %) 1 (20 %)	0.766

DKA=diabetic ketoacidosis

CONCLUSION

Our study clearly demonstrates that diabetes among hospitalized patients with COVID-19 puts them at higher risk of morbidity and mortality. This was especially associated with uncontrolled fasting hyperglycemia (>7mmol/L). Effective measures such as implementation of hyperglycemia algorithm for hospitalized patients and follow up plan should be implemented. This may improve the length of hospital stay and the outcomes in COVID-19 patients.

REFERENCES

1. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet, 2020.
2. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA, 2020; 323: 1061–9. https://doi.org/10.1001/jama.2020.1585.
3. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA, 2020; 323: 2052–9. https://doi.org/10.1001/jama.2020.6775.
4. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. International Journal of Infectious Diseases, 2020.
5. Deng S-Q, Peng H-J. Characteristics of and public health responses to the coronavirus disease 2019 outbreak in China. Journal of Clinical Medicine, 2020; 9: 575.
6. Zhang J, Dong X, Cao Y, Yuan Y, Yang Y, Yan Y, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy, 2020.
7. Zhu L, She Z-G, Cheng X, Qin J-J, Zhang X-J, Cai J, et al. Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes. Cell Metabolism, 2020; 31: 1068-1077.e3. https://doi.org/10.1016/j.cmet, 2020; 04: 021.
8. Xu M, Liu PP, Li H. Innate immune signaling and its role in metabolic and cardiovascular diseases. Physiological Reviews, 2019; 99: 893–948.
9. Kumar Nathella P, Babu S. Influence of diabetes mellitus on immunity to human tuberculosis. Immunology, 2017; 152: 13–24.
10. Alqahtani FY, Aleanizy FS, Mohamed RAEH, Alanazi MS, Mohamed N, Alrasheed MM, et al. Prevalence of comorbidities in cases of Middle East respiratory syndrome coronavirus: a retrospective study. Epidemiology & Infection, 2019; 147.
11. Yang JK, Feng Y, Yuan MY, Yuan SY, Fu HJ, Wu BY, et al. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. Diabetic Medicine, 2006; 23: 623–8.
12. Booth CM, Matukas LM, Tomlinson GA, Rachlis AR, Rose DB, Dwosh HA, et al. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. Jama, 2003; 289: 2801–9.
13. MOH S. Supportive care and antiviral treatment of suspected or confirmed COVID-19 infection. Version, 2020. https://www.moh.gov.sa/Ministry/MediaCenter/Publications/Documents/MOH-therapeutic-protocol-for-COVID-19.pdf.
14. Sanyaolu A, Okorie C, Marinkovic A, et al. Comorbidity and its Impact on Patients with COVID-19 [published online ahead of print, 2020 Jun 25]. *SN Compr Clin Med*, 2020; 1-8. doi:10.1007/s42399-020-00363-4
15. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: prevalence, pathophysiology, prognosis, and practical considerations. Diabetes Metab Syndr Clin Res Rev, 2020; 14(4): 303–10. [Accessed April 18, 2020,\.
16. W.-J. Guan, Z.-Y. Ni, Y. Hu, W.-H. Liang, C.-Q. Ou, J.-X. He, *et al.* Clinical characteristics of coronavirus disease 2019 in China N Engl J Med, 2020. 10.1056/NEJMoa2002032
17. Rees, E.M., Nightingale, E.S., Jafari, Y. *et al.* COVID-19 length of hospital stay: a systematic review and data synthesis. *BMC Med*, 2020. https://doi.org/10.1186/s12916-020-01726-3
18. W.-J. Guan, Z.-Y. Ni, Y. Hu, W.-H. Liang, C.-Q. Ou, J.-X. He, *et al.* Clinical characteristics of coronavirus disease 2019 in China N Engl J Med, 2020. 10.1056/NEJMoa2002032
19. Bode B, Garrett V, Messler J, McFarland R, Crowe J, Booth R, Klonoff DC. Glycemic Characteristics and Clinical Outcomes of COVID-19 Patients Hospitalized in the United States. J Diabetes Sci Technol, 2020; 14(4): 813-821.
20. Goldman N, Fink D, Cai J, Lee YN, Davies Z. High prevalence of COVID-19-associated diabetic ketoacidosis in UK secondary care. *Diabetes Res Clin Pract*, 2020; 166: 108291. doi:10.1016/j.diabres.2020.108291
21. Armeni E, Aziz U, Qamar S, et al. Protracted ketonaemia in hyperglycaemic emergencies in COVID-19: a retrospective case series. *Lancet Diabetes Endocrinol*, 2020; 8(8): 660-663. doi:10.1016/S2213-8587(20)30221-7
22. Matthew C. Riddle, John B. Buse, Paul W. Franks, William C. Knowler, Robert E. Ratner, Elizabeth Selvin, Deborah J. Wexler, Steven E. Kahn COVID-19 in People With Diabetes: Urgently Needed Lessons From Early Reports.Diabetes Care, 2020; 43(7): 1378-1381. DOI: 10.2337/dci20-0024
23. Palermo NE, Sadhu AR, McDonnell ME. Diabetic Ketoacidosis in COVID-19: Unique Concerns and Considerations. *J Clin Endocrinol Metab*, 2020; 105(8): 360. doi:10.1210/clinem/dgaa360

24. Wang S, Ma P, Zhang S, et al. Fasting blood glucose at admission is an independent predictor for 28-day mortality in patients with COVID-19 without previous diagnosis of diabetes: a multi-centre retrospective study. Diabetologia, 2020; 63(10): 2102. DOI: 10.1007/s00125-020-05209-1.
25. Yehualashet AS, Belachew TF. ACEIs and ARBs and Their Correlation with COVID-19: A Review. Infect Drug Resist, 2020; 13: 3217-3224. https://doi.org/10.2147/IDR.S264882