



RESEARCH ARTICLE

CLINICAL COURSE AND DISEASE OUTCOME IN COVID-19 PATIENTS WITH DIABETES MELLITUS

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Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19) whose pandemic was declared on March 11 2021 (1). Spectrum of COVID-19 clinical manifestations is very wide. Most patients report to ambulance with mild or moderate symptoms, but some of them rapidly develops acute respiratory distress syndrome (ARDS), respiratory failure, acute cardiac injury, multiple organ failure and death (2). Older age, diabetes mellitus and cardiovascular disease are reported as high predictors of morbidity and mortality.

Aim: To determine correlation between diabetes mellitus and severity of clinical picture in patients with COVID-19.

Methods: Current study involve retrospective analysis of 1513 patients with Real Time PCR confirmed COVID-19 hospitalized in Clinic for infectious disease, University Clinical Centre, Sarajevo, Bosnia and Herzegovina, in a period of June 2020 to December 2020.

Results: Among them 417 had previously diagnosed of diabetes mellitus. Results show that patients with diabetes mellitus are likely to require treatment in Intensive care unit, and oxygenic support with invasive ventilation. There was no statistically significant difference in outcome of the disease.

Conclusion: Even this study didn't find increased mortality in patients with COVID-19 and diabetes mellitus, further studies should be done to determine risk for patients with DM to develop severe form of disease.

Keywords: COVID-19, Diabetes mellitus, outcome.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a virus that causes coronavirus disease 2019 (COVID-19). Pandemic of COVID-19 was declared in March 2020¹. Spectrum of COVID-19 clinical manifestations is very wide. Patients usually present with mild or moderate symptoms, but some of them can develop acute respiratory distress syndrome (ARDS). Also, other manifestations like respiratory failure, acute cardiac injury, multiple organ failure and death have been observed². Significant predictors of morbidity and mortality are older age, diabetes and cardiovascular disease.

Diabetes mellitus (DM) is considered to be one of the leading causes of morbidity and mortality throughout the world. Diabetes mellitus can cause macrovascular and microvascular complications, that impact the patient's survival³. A strong relationship between diabetes and infection has been already recognized, and

patients with DM have great susceptibility to infections with bad prognosis⁴. It is yet unclear whether diabetes increases susceptibility to infections and affects its outcomes, or main reasons are complications usually associated with DM, like renal or cardiovascular complications⁵. Diabetes is reported as significant predictor of severity and mortality rate in patients infected with different kind of infections, including the pandemic influenza, SARS and MERS^{6,7,8}. There is no study that can confirm independent predictive value of diabetes on outcome and mortality in COVID-19 patients⁹. Diabetes is hyper-inflammatory condition and has ability to increase susceptibility for COVID-19. Potential mechanisms include higher affinity cellular binding with efficient virus entry, decreased viral clearance, diminished T-cell function and increased possibility to cytokine storm¹⁰. Coronavirus infections have a huge effect on the management of DM because they aggravate inflammation and also alter immune system responses, leading to difficulties

in glycaemic control¹¹. SARS-CoV-2 virus uses ACE2 as entry receptors, which can cause mild to severe damage to these cells, leading to different clinical condition¹².

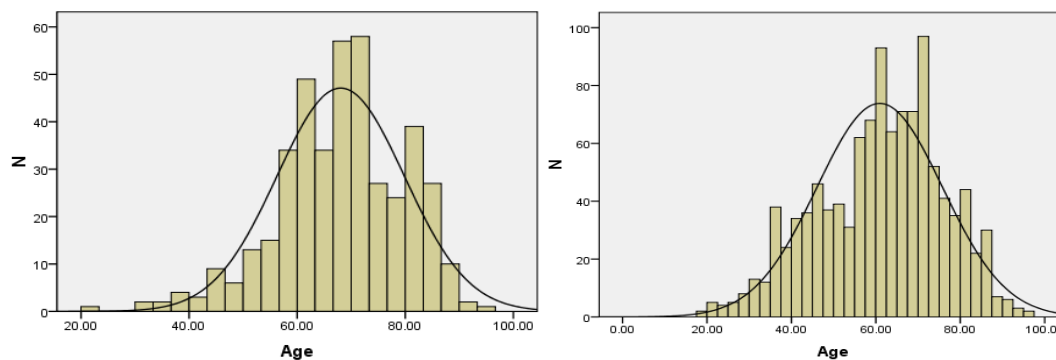
SUBJECTS AND METHODS

This is an observational retrospective study of adult patients with COVID-19 and diabetes mellitus admitted to Clinic for infectious disease, University Clinical Center, Sarajevo, Bosnia and Herzegovina, in a period of June 2020 to December 2020, which is approved in 2020, reference number 3886/20. Inclusion criteria were laboratory-confirmed diagnosis of COVID-19 based on Real-Time PCR, age of patients 18 years and above, medical record of previously diagnosed DM. Exclusion criteria were diagnosis based only on rapid antigen test, age under 18 years, and newly discovered diabetes. Data were retrieved from the patient's history records: age, sex, duration of symptoms before hospitalisation, length of hospitalisation, and requirement for oxygen support via facial mask, requirement to admission in Intensive

Care Unit (ICU) with requirement for invasive ventilation, and the outcome of disease. Since this was an observational study without any implication to patient's treatment or personal data, there was no need for informed consent. Patient population was divided into two categories based on their history of diabetes: without diabetes and previously known cases of diabetes. Current study used descriptive and non-parametric statistical methods for the results interpretation.

Statistical analysis

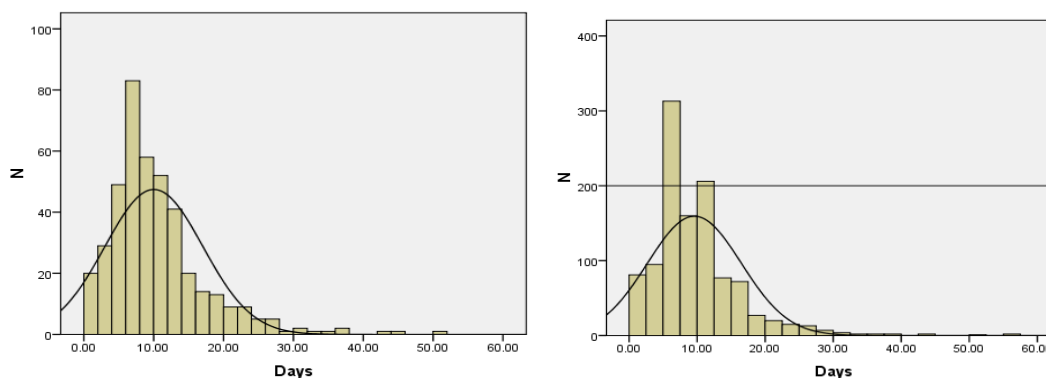
Statistical analysis was conducted using Pearson's Chi square test for comparison of non-parametric values. There was no statistically significant difference in age of admitted patients between groups (Pearson's Chi square =46.81, $p=0.15$). Duration of hospital stay had statistically significant difference between groups (Pearson's Chi square =18.68, $p<0.001$), as well as admission in ICU (Pearson's Chi square =18.68, $p = 0.005$). There was no statistically significant difference between groups for outcome of the disease (Pearson's chi square=0.05, $p=0.84$).



A. With diabetes mellitus.

B. Without diabetes mellitus.

Figure 1: Age of patients admitted to the hospital for both groups.



A. With diabetes mellitus.

B. Without diabetes mellitus.

Figure 2: Duration of hospital stay for both group of patients.

RESULTS

In a period of June 2020 to December 2020 total of 1792 patients were hospitalised in Clinic for infectious diseases in Sarajevo. Out of that number, 1513 patients had COVID-19, confirmed with positive PCR test for SARS-CoV-2. For the statistical analysis we divided them into two groups: with or without diabetes mellitus as underlying disease. In group with DM we had 417

(27.5%) patients and in the group without DM there were 1102 (72.5%) patients. Mean age in group with DM was 68 years (SD=11.17, range 22-96 years) and in a group without DM was 62 years (SD=14.86, range 19-95 years). In both groups males were mostly presented -61.4 vs 38.6% in group with DM, and 66.3 vs 32.7% in a group without DM. In a group with DM there was 61.4% of male and 38.6% of female patients (Figure 1). Duration of presented symptoms before

admission to hospital was in range 1 to 20 days (Me 7.96, SD=3.76) in a group with DM and in range 1-24 days (Me 7.86, SD=3.70) in a group without DM. Duration of hospital stay for a group with DM ranged 1 to 50 days (Me 10.02, SD=7.01), and in group without DM in range 1 to 90 days (Me 9.59, SD=6.89) (Figure 2).

Table 1: Requirement for oxygenation via facial mask.

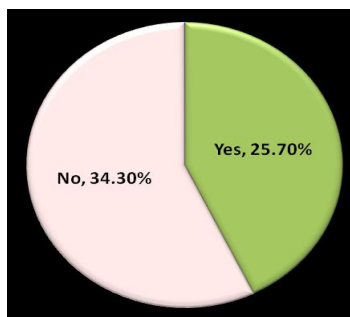
		Yes (%)	No (%)
DM	With	355 (85.1%)	62 (14.9%)
	Without	824 (74.7%)	278 (25.3%)
Total		1179 (77.6%)	340 (22.4%)

Total 85.1% patients in a group with DM required oxygenic support via facial mask while that number in a group without DM was 74.7%, with statistical

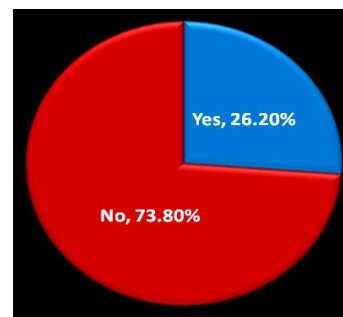
difference between groups (Pearson's Chi square=18.68, $p<0.001$) (Table 1). Admission in intensive care unit (ICU) and oxygen support with respiratory machine (invasive ventilation), required 23.3% in a group with DM, while in group without DM that number was 13.1% (Table 2). In a group with DM we had total of 107 (25.7%) lethal outcomes and in a group without DM we had total 289 (26.2%) lethal outcomes. Other patients were discharged from hospital as recovered (Figure 3).

Table 2: Requirement for mechanical ventilation.

		Yes (%)	No (%)
DM	With	79 (23.3%)	338 (76.7%)
	Without	145 (13.1%)	957 (86.9%)
Total		224 (14.7%)	1295 (85.3%)



A. With diabetes mellitus.



B. Without diabetes mellitus.

Figure 3: Outcome of disease for patients in both groups.

DISCUSSION

Diabetes mellitus is recognised as one of possible risk factors for developing serious form of COVID-19. Since mortality from diabetes is in constant increase in Bosnia and Herzegovina in the last 10 years, this could be one of the reasons for very high morbidity and mortality for COVID-19 among citizens¹³. In a period, of July 2020–December 2020, total 1513 patients were admitted to Clinic for infectious diseases, Clinical centre University of Sarajevo. Most of them were with moderate to severe clinical presentation, since mild and asymptomatic forms are treated through Primary care. There were very large proportion of patients with previously detected diabetes (27.5%). In two largest meta-analyses that included 46 248 and 76 993 COVID-19 patients, respectively, diabetes was detected in 8.6% and 7.9%^{14,15}. The same group of authors in a larger group of COVID-19 patients (n=1590) reported diabetes in 8.2%, and it was significantly more prevalent in a group of COVID-19 patients with severe form than in patients with mild or moderate form of disease (34.6% vs 14.3%)¹⁶. Median age of patients in this study with diabetes was 68 years, and without diabetes 62 years. Study conducted by Guo *et al.*, also showed there was no significant difference in age between patients with DM and non-diabetics¹⁷. There was significant difference between sex of admitted patients, since the ratio was around 2:1 for males vs. females. But, in similar study led by

Hafidh *et al.*, the percent of males with diabetes was 94%¹⁸. Guo *et al.*, also proved that diabetes was significantly more prevalent in patients who were admitted in intensive care, required mechanical ventilation, with fatal outcome, than in patients who did not have these complications (26.9% vs 6.1%)¹⁹. Wang *et al.*, conducted a study including 1558 patients which proved diabetes is associated with severity of clinical presentation, but they did not find correlation with admission in intensive care unit²⁰. Chen *et al.*, in the study of DM prevalence in COVID-19 patients concluded that percent of patients with DM with fatal outcome was 21% and with favourable outcome 14%. Also they found 23.7% patients in a group with DM required non-invasive or invasive ventilation, and in group without DM that number was lower, 19.4%²¹. A study from UAE found mortality of 10% among COVID-19 patients with DM. It also notified that the mortality and requirement for mechanical ventilation were higher for the patients with newly diagnosed DM in comparison with patients who had DM before admission¹⁸. Meta-analysis from Wu *et al.*, found significant relation of mortality in COVID-19 patients with pre-existing diabetes, OR of 1.75 (95% CI 1.31–2.36; $p=0.0002$)²². In this study there was statistically significant difference in outcome for patients with and without diabetes mellitus, ($p=0.84$).

CONCLUSIONS

Diabetes mellitus is underlying disease that can lead to development of severe form of COVID-19. Most of the patients will require admission to ICU and mechanical ventilation. This study did not find increased mortality in patients with COVID-19 and diabetes mellitus, but other studies suggest it is likely to be. Further studies should be done to determine exact risk for development of severe clinical forms and unfavourable outcome in patients with diabetes and COVID-19.

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AUTHOR'S CONTRIBUTION

Baljic R: writing original draft, methodology. **Velic A:** literature survey. **Muhic A:** interpretation of data. **Gojak R:** data curation, conceptualization. **Gazibera B:** interpretation of data. **Bajramovic N:** editing, methodology. **Hadzovic-Cengic M:** critical review. **Huric I:** editing, methodology. All authors revised the article and approved the final version.

DATA AVAILABILITY

Data will be made available on reasonable request.

CONFLICT OF INTEREST

No conflict of interest associated with this work.

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