

## **Response to Referees:**

### **Referee 1:**

#### **1. Novelty of Findings.**

Our findings may appear less novel than expected, but this is a carefully performed study containing important information on a timely topic. COVID-19 patients with T2D died from COVID-19 at 3 times the rate of patients without T2D. Old age, increased WBC and elevated serum troponin were identified as predictors of mortality in patients with and without T2D. However, only lymphopenia has been identified as a predictor of mortality among Covid-19 patients with T2D. It seems that the increased severity and mortality of patients with COVID-19 and T2D is due to severe proinflammatory state with cardiac injury in older patients with comorbidities such as hypertension, CVD, CKD, and obesity.

#### **2. Methods**

In addition to the Kaplan-Meier analysis of the effect of T2D on survival, univariate and multivariate analysis, containing all the variables that differed statistically between survivors and non-survivors were performed to identify the independent predictors of mortality among Covid-19 patients with T2D.

Most laboratory and radiographic severity indices of COVID-19 non-survivors were high in both patients with and without T2D. But on univariate analysis of independent predictors of mortality among T2D non-survivors, significant associations were identified with old age, increased WBC, leukopenia, and elevated serum troponin. On using Multivariate analysis only leukopenia was identified as an independent predictor of mortality among T2D non-survivors

#### **3. Composition of Report.**

The data obtained and reported in the Abstract, Results and Discussion Sections have been revised after the use of both univariate and multivariate analysis. No contradiction can be seen in the new version.

### **Referee 2:**

#### **1. Relationship between glycaemic control and outcome.**

The relationship between random blood glucose, fasting blood glucose and blood Hb<sub>A1C</sub>, with mortality, among COVID-19 patients with T2D, was tested using Mann Whitney U test and found to be insignificant.

#### **2. Limitation of cross-sectional Study.**

The authors acknowledge several limitations. It is possible that there was selection bias in this study, as this is a short-term cross-sectional nested case-control study where data were collected over a short period in a pandemic environment. Also, in this cross-sectional study it is not possible to establish causal inference or analyse temporal changes.

#### **3. How to distinguish between Type 1 and Type 2 diabetes.**

All patients with type 1 diabetes were excluded. This was based on their previous history on the SALAMA Electronic Health Records System and confirmed on admission.

4. English editing.

Elsevier Service was used to polish English language.

**Referee 3:**

1. Limitation of cross-sectional Study to infer causality and observe changes over time.

The authors acknowledge several limitations. It is possible that there was selection bias in this study, as this is a short-term cross-sectional nested case-control study where data were collected over a short period in a pandemic environment. In this cross-sectional study it is not possible to establish causal inference or analyse temporal changes.

2. Single centre limit generalizability of finding.

We agree with the Referee. But during the Pandemic four main centres were designated for isolation and admission of all COVID-19 patients in the Emirate of Dubai. Dubai Hospital, where the study was conducted, was one of those centres. Most of the hospital wards were converted into isolation units to accommodate patients with COVID-19. Thousands of patients with COVID-19 were admitted to Dubai Hospital during 2020. In this cross-sectional nested case-control study, only 1092 patients were recruited between the period of March 21<sup>st</sup> till September 30<sup>th</sup>, 2020.

3. Random sampling and introduction of selection bias.

Could not be avoided. It is an observational study.

4. Impact of different treatment protocols on outcomes.

Management and Treatment of COVID-19 followed UAE Guidelines.<sup>28</sup> which were based on NIH guidelines (NIH, 2021).<sup>29</sup> After a thorough assessment of clinical severity, all COVID-19 patients were treated at the time (March-September 2020) with a standard combination of Hydroxychloroquine Sulphate and Kaletra antiviral (Lopinavir/Ritonavir). So, there were no differences in the drug management of both patients with and without T2D.

5. Potential confounders.

The relationship between random blood glucose, fasting blood glucose and blood Hb<sub>A1C</sub>, and mortality among patients with COVID-19 and T2D was tested using the Mann-Whitney U test and found to be statistically insignificant. Therefore, hyperglycaemia *per se* does not seem to be an independent predictor of mortality. On the contrary, it seems that mortality of T2D patients is driven by a much higher proinflammatory response to COVID 19 as evidenced by higher CRP, higher WBC, with lymphopenia and cardiac injury as evidenced by a raised level of serum troponin. It is also possible that mortality is synergized by a large number of comorbidities and complications associated with T2D patients in advancing age.