Diabetology

Extended Abstract

Glycosylated hemoglobin is associated withsystemic inflammation, hypercoagulability, andprognosis of COVID-19 patients- Fengxue Zhu - Peking University People's Hospital, Beijing , China

Fengxue Zhu

Abstract

Background:Diabetes is a risk factor for the progression and prognosis of coronavirus dis-ease (COVID-19), but the relationship between glycosylated hemoglobin (HbA1c) level,inflammation, and prognosis of COVID-19 patients has not been explored.Methods:This was a retrospective study of COVID-19 patients who underwent an HbA1ctest. Their demographic data, medical history, signs and symptoms of COVID-19, laboratorytest results, and final outcomes of COVID-19 treatment were collected and analyzed.Results:A total of 132 patients were included and divided into three groups based on theirblood glucose status. There were significant differences in SaO2, serum ferritin level, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen (Fbg) level, andIL6 level among the three groups. A pairwise comparison of the groups showed that groupsB and C were significantly different from group A in terms of CRP, ESR, and Fbg, IL6, andserum ferritin levels ($P < 0.05$). Correlation analysis showed that there was a linear negativecorrelation between SaO2and HbA1c ($r = 0.22$, $P = 0.01$), while there was a linear positivecorrelation between serum ferritin, CRP, Fbg, and ESR levels and HbA1c ($P < 0.05$).Conclusions:High HbA1c level is associated with inflammation, hypercoagulability, and lowSaO2in COVID-19 patients, and the mortality rate (27.7%) is higher in patients with dia-betes. Determining HbA1c level after hospital admission is thus helpful assessing inflam-mation, hypercoagulability, and prognosis of COVID-19 patients.

A total of 132 patients tested positive for COVID-19 by under-going the SARS-CoV-2 RNA test were included in our study.The median age of the patients was 66 years (IQR 56–72 years),ranging from 24 to 88 years. The number of men was 68, whilethe number of women was 64. A total of 88 (66.7%) of thepatients had comorbidities, of which hypertension was themost common (50.0%), followed by diabetes (35.6%), cardio-vascular or cerebrovascular disease (24.2%), and chronic kid-ney disease (7.6%). Seven patients had chronic renal failureundergoing long-term maintenance hemodialysis andreceived intermittent renal replacement therapy (IRRT) atbedside during hospitalization. The median time from onsetto admission was 14 (IQR 10.0–17.8) days. SaO2was 95% (IQR90–97%) without oxygen inhalation at the time of admission,ranging from 59% to 99% (Table 1).The median HbA1c level was 6.4 (IQR 5.8–7.2%), and therewere significant differences among the groups with regard tovarious parameters including SaO2, serum ferritin, CRP, ESR,fibrinogen (Fbg), and IL6 levels ($P < 0.01$,Table 2). A pairwisecomparison within the groups showed that the differencesbetween groups C and A, and groups B and A were statisticallysignificant in terms of ESR, CRP, serum ferritin, Fbg, and IL6levels (Fig. 1). Correlation analysis revealed that there was alinear negative correlation between SaO2and HbA1c, whilethere was a linear positive correlation between serum ferritin,CRP, Fbg, and ESR levels and HbA1c (Fig. 2).A total of 22 patients died (16.7%) during hospitalization,including 4 deaths in group A (9.8%), 5 deaths in group B(11.40%), and 13 deaths in group C (27.7%); All patients under-went terminal withdrawal of mechanical ventilation. Therewas a statistically significant difference between groups Aand C in terms of mortality rate ($P = 0.03$,Table 3

In our study, owing to the presence of acute viral infections,we did not consider HbA1c as the diagnostic standard for dia-betes, according to the guidelines[5]. This is the first study toreport that diabetic patients contracting COVID-19 have moresevere inflammation and higher mortality[6], and thatinflammations markers such as serum ferritin level, CRPlevel, and ESR in COVID-19 cases and the coagulation

Fengxue Zhu
Peking University People's Hospital, Beijing ,China, E-mail: xzhu72@126.com

factorFbg were positively correlated with HbA1c level, while SaO2was negatively correlated with HbA1c level. Even in patientswith only elevated HbA1c level and no diabetes, the levelsof inflammation markers and Fbg were also significantlyincreased (Fig. 1, $P < 0.05$). However, little is known aboutthe mechanism concerning the increase in the levels ofinflammation markers and HbA1c level in case of COVID-19patients. Previous studies have shown that diabetes not onlycauses epithelial dysfunction of pulmonary cilia, increasedvascular system permeability, alveolar epithelial damage,and alveolar collapse but also contributes to abnormalimmune system function[7,8]. Similarly, in severely illCOVID-19 patients, the lungs, spleen, and lymph node struc-tures are damaged, and lymphocyte counts are reduced[9].Both diabetes and COVID-19 may synergistically damage the immune and respiratory systems. Further, diabetic patientshave more comorbidities due to which there is more targetorgan damage; this together with COVID-19 leads to a moresevere inflammation, hypercoagulability, an even low oxy-genation, and eventually higher mortality.COVID-19 patients with higher HbA1c level may exhibitrelatively higher level of severity, and the infection itselfmay also lead to an increase in HbA1c level. Previous studieshave also found that in severe acute respiratory syndrome(SARS) patients, even those with mild symptoms (who donot receive glucocorticoid therapy during the course of thedisease), had higher fasting blood glucose levels[10]. In ourstudy, after excluding treatment with exogenous corticos-teroids, hemolysis, the HbA1c level of 66.7% (88/132) patientswas still higher than normal (4.0–6.0%), of which 12.1%(16/132) patients were newly diagnosed with diabetes. Forthe new-onset diabetes patients, previously reported studiesalong with this study suggest that COVID-19 may cause andaggravate abnormal glucose metabolism.The possible mechanisms of COVID-19 causing abnormalglucose metabolism include isletbcell damage and insulinresistance. Previous studies have reported that some virusescan directly cause pancreaticb-cell damage[11,12], andangiotensin converting enzyme 2 (ACE2) as a SARS-CoV-2receptor has higher expression in pancreatic endocrine tis-sues than in exocrine tissues[13]. Autopsy showed thatalthough a small number of islet cells were degenerated inpancreatic tissue, while immunohistochemical analysis andpolymerase chain reaction tests did not detect the presenceof SARS-CoV-2 in pancreatic islet cells[9], thus indicating thatthere is insufficient evidence regarding SARS-CoV-2-induceddamage of islet cells. Levels of plasminogen activator inhibi-tor 1, CRP, serum amyloid A, TNF-a, IL-1b, and IL-6 have beenshown to be increased in obese and type 2 diabetic patients.IL-1bcan cause isletbcell dysfunction and apoptosis, andthe levels of these factors can be reduced by lifestyle-relatedchanges and weight loss, which suggests that inflammatorymarkers may be involved in isletbcell damage and insulinresistance[14]. Inflammatory factors released in response toSARS-CoV-2 may also be involved in isletb-cell damage andinsulin resistance resulting in abnormal glucose metabolism.In our study, patients had 14 (IQR 10.0–17.8) days from theonset of symptoms to admission. Abnormal glucose metabo-lism for a long period of time may cause an increase in HBV1clevel.

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