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Association between Use of Metformin and Insulin with Hematological Parameters in COVID-19 Patients with Type 2 Diabetes: A Single Center, Cross-Sectional Study

Coronavirus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was first reported in December 2019 [1].

Type 2 diabetes (T2D) is an important risk factor for mortality and poor prognosis in COVID-19 patients [2, 3]. Metformin and insulin were suggested to have an impact on the outcomes. However, opposing viewpoints continue to be expressed. In this study, we sought to perform a retrospective analysis of metformin and insulin effects in COVID-19 patients with T2D.

This was a retrospective study conducted at the Transcarpathian Regional Clinical Infectious Diseases Hospital (Uzhhorod, Ukraine). We used retrospective patient data collected from medical records available from the e-health information system, which included all adult patients admitted from January 2021 to March 2022. Confirmation of the diagnosis of COVID-19 was carried out by the PCR method. In-hospital confirmed COVID-19 patients were divided into T2D and non-diabetes. T2D was defined according to the World Health Organization diagnostic criteria [4].

The results are reported as the median [interquartile range (IQR)] for baseline laboratory indices and the number [percentage] for categorical variables. The classification variable was represented as a count (%). Continuous variables with normal distribution were presented as mean [standard deviation (SD)]. Differences in parameters among groups were analyzed using ANOVA for continuous variables, and the χ^2 test was used for categorical variables. P-value ≤ 0.05 was considered to indicate statistical significance.

Among the 145 confirmed patients, the median age was 62.66 ± 12.96, and 66 patients (45.5%) were male. Patients with T2DM were older than patients without T2D 53.66 ± 13.37 vs. 67.00 ± 7.70 ($p = < 0.001$). Among these 80 diabetic patients, all had T2D.

During hospitalization, 25 cases with T2D had metformin. Patients had in-hospital metformin with a median of 1.0 g per day (IQR 0.55–1.52). In patients who took metformin, the level of C-reactive protein (CRP) was significantly lower than in patients who did not take metformin [24 mg/L (IQR 15–58) vs. 52 mg/L, (IQR 22–121), $p = 0.046$] (Tab. 1).

After admission, 35 patients received insulin. In-hospital insulin users with a median of 35.0 units per day

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Table 1. Characteristics of Baseline Laboratory Indices in Metformin or Insulin Users

Characteristics	Non-metformin (N = 16)	Metformin (N = 25)	P-value	Non-insulin (N = 10)	Insulin (N = 35)	P-value
Age [years]	58.67 ± 10.81	60.80 ± 12.56	0.518	52.67 ± 8.81	67.8 ± 9.26	0.038
Gender (M, %)	7 (43.7 %)	12 (48 %)	0.657	6 (60 %)	17 (48.5 %)	
Comorbidities (n, %)						
Hypertension, N (%)	7 (43.7%)	7 (28%)	0.257	3 (30%)	9 (25.7%)	0.436
Cardiovascular disease, N (%)	2 (12.5%)	4 (16%)	0.368	1 (10%)	5 (14.2%)	0.813
Chronic kidney disease, N (%)	7 (43.7%)	7 (28%)	0.537	4 (40%)	10 (28.5%)	0.251
Baseline laboratory indices						
Blood glucose [mmol/L]	7 (5–14)	10 (8–14)	0.014	5 (4–8)	14 (9–15)	< 0.001
White blood cells [× 10^9/L]	8 (6–12)	9 (6–10)	0.463	7 (5–11)	9 (7–12)	0.082
Lymphocytes [× 10^9/L]	1 (1–1)	1 (1–1)	0.666	1 (1–2)	1 (1–1)	0.430
Monocytes [× 10^9/L]	0 (0–0)	0 (0–0)	0.040	0 (0–0)	0 (0–0)	0.368
Neutrophils [× 10^9/L]	7 (5–11)	7 (4–9)	0.315	6 (4–8)	9 (6–11)	0.022
Serum creatinine [μmol/L]	102 (86–119)	105 (90–124)	0.644	102 (86–118)	102 (87–127)	0.647
C-reactive protein [mg/L]	52 (22–121)	24 (15–58)	0.046	40 (16–104)	43 (18–100)	0.846
D-dimer [μg/mL]	1 (0–3)	1 (0–3)	0.544	1 (0–3)	2 (1–3)	0.181
Procalcitonin [ng/mL]	0 (0–1)	0 (0–1)	0.660	0 (0–1)	0 (0–1)	0.340
COVID-19 treatment protocols						
Antibiotics (n, %)	13 (81.2%)	14 (56%)	0.486	8 (80%)	25 (71.4%)	0.587

(IQR 28.2–50.3). Higher blood glucose levels [14 mmol/L, (IQR 9–15) vs. 5 mmol/L (IQR 4–8), p = < 0.001] were seen in insulin users. Patients in the insulin group had higher white blood cell (WBC) count [9 × 10^9/L, (IQR 7–12) vs. 7 × 10^9/L (IQR 5–11), p = 0.082] and neutrophil levels than those of the non-insulin group [9 × 10^9/L, (IQR 6 –11) vs. 6 × 10^9/L (IQR 4–8), p = 0.022] with no difference in general characteristics and other laboratory indices.

In this study, we found that metformin use prior to admission was linked to declining CRP levels among COVID-19 patients with T2D. In the long run, metformin may be more advantageous than insulin for COVID-19 patients with T2D. To confirm the current findings, more research is required.

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Conflict of interest

None declared.

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