CORRESPONDENCE

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Coronavirus disease 19 and risk of hyperglycemia among Iraqi patients

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Abstract

A cross-sectional observational study was conducted on 213 patients with COVID-19 who did not have a clinical history of diabetes at hospital admission. One week after hospitalization, they were stratified by random blood glucose levels. It was found that 25.4, 22.5 and 52.1% of COVID-19 patients were classified as normoglycemia, prediabetes and diabetes, respectively. The study indicated that diabetes may be a risk factor for COVID-19 or the disease may be associated with an increased risk of developing diabetes.

Keywords: COVID-19, Diabetes, Hyperglycemia, Prediabetes, Random blood glucose

The World Health Organization (WHO) and health authorities have devoted significant attention to understanding risk factors for coronavirus disease 19 (COVID-19) and their role in disease outcomes [1]. Several predictors were identified by a comparative analysis of risk factors across 17 studies, and age and diabetes were considered to be highly consistent [2]. Additional data support the concept that diabetes and other related diseases (hypertension and cardiovascular diseases) are the most common comorbidities in COVID-19 patients [3, 4]. It has also been proposed that COVID-19 is likely associated with an increased risk of developing diabetes [5]. This motivated us to conduct a study to explore the incidence of diabetes in hospitalized COVID-19 cases.

A multicenter cross-sectional observational study was conducted on 213 patients diagnosed with COVID-19 at referral hospitals for the management of COVID-19 in Baghdad during the period from 1 October to 15 November 2020. COVID-19 was molecularly diagnosed by detection of virus RNA in patients' nasopharyngeal secretions (reverse transcription–polymerase chain reaction test). The included patients were those who did not have a clinical history of diabetes when they were admitted to hospitals. One week after hospitalization, the records of these patients were inspected for age, gender, body mass index (BMI), ABO and Rh blood groups, hemoglobin (Hb), platelet count, white blood cell count (WBC), erythrocyte sedimentation rate (ESR), random blood glucose (RBG), and serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total cholesterol, triglycerides, creatinine and blood urea nitrogen.

Continuous variables were given as mean and standard deviation (SD), and one-way analysis of variance (ANOVA) followed by Duncan's multiple-range post hoc test was used to assess significant differences. Categorical variables were expressed by number and percentage, and Pearson Chi-squared test was used to assess significant differences. A probability value (p) ≤ 0.05 was considered significant. The IBM SPSS Statistics 25.0 (Armonk, NY: IBM Corp.) was used to perform these analyses.

The mean age of COVID-19 patients was 57.4 ± 15.3 years. Males outnumbered females (86.4 *vs.* 13.6%). Most patients were overweight/obese (79.8%). Blood group O was the most common (37.6%), followed by blood groups A, B and AB (31.5, 21.6 and 9.4%, respectively). Rh-negative phenotype was present in 16.9% of patients. Other laboratory data were either within the normal range (Hb, platelets, ALT, AST and

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ALP) or above (WBC, ESR, and RBG). The RBG was higher than the normal range (269.5 ± 179.4 vs. 79 to <140 mg/dL). Thus, hyperglycemia might have been identified in COVID-19 patients. This finding prompted us to re-examine the RBG and categorize patients into normoglycemia (79 to <140 mg/dL), prediabetes (140–199 mg/dL) and diabetes (≥ 200 mg/dL) according to the American Diabetes Association criteria [6]. It was found that 25.4% of COVID-19 patients were classified as normoglycemia, 22.5% as prediabetes and 52.1% as diabetes. It was also noted that the mean age paralleled the categorization gradually; 53.2 ± 16.8 years for normoglycemia, 55.6 ± 15.7 years for prediabetes and 60.4 ± 13.7 years for diabetes, and the difference was significant (p value $= 0.01$). As for gender, BMI and blood groups, their distribution in the three groups of patients did not show significant differences. The blood parameters also showed no significant differences between normoglycemia, prediabetes and diabetes. Platelets, RBG and ALP were exceptions and showed significant differences between the three groups of patients (Table 1 and Fig. 1).
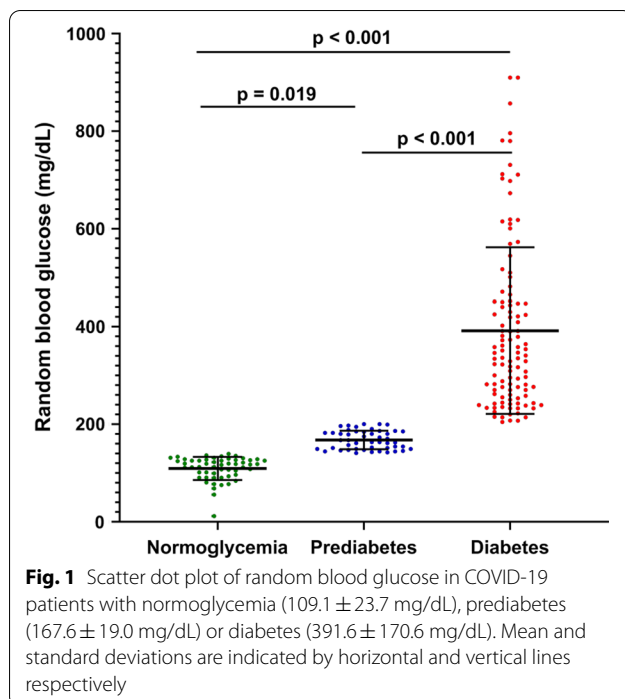
The main interest of this study was to observe if COVID-19 in general is linked to an altered RBG or diabetic condition. The results indicated that this infection was associated with an increased incidence of diabetes or diabetes may be a risk factor for the development of COVID-19. Some COVID-19 patients might have developed hyperglycemia after hospitalization, while their clinical history did not indicate any evidence of diabetes;

Table 1 Characteristics of COVID-19 patients

Characteristic	All patients $N = 213$	Normoglycemia $N = 54$	Prediabetes $N = 48$	Diabetes $N = 111$	*p* value
Age; year	57.4 ± 15.3	53.2 ± 16.8^B	55.6 ± 15.7^{AB}	60.4 ± 13.7^A	**0.01**
Gender					
Male	184 (86.4)	47 (87.0)	43 (89.6)	94 (84.7)	0.701
Female	29 (13.6)	7 (13.0)	5 (10.4)	17 (15.3)	
BMI					
Normal-weight	43 (20.2)	12 (22.2)	7 (14.6)	24 (21.6)	0.544
Overweight/obese	170 (79.8)	42 (77.8)	41 (85.4)	87 (78.4)	
Blood group					
O	80 (37.6)	23 (42.6)	15 (31.3)	43 (38.7)	0.587
A	67 (31.5)	15 (27.8)	15 (31.3)	36 (32.4)	
B	46 (21.6)	12 (22.2)	10 (20.8)	24 (21.6)	
AB	20 (9.4)	4 (7.4)	8 (16.7)	8 (7.2)	
Rh					
Negative	36 (16.9)	10 (18.5)	6 (12.5)	20 (18.0)	0.650
Positive	177 (83.1)	44 (81.5)	42 (87.5)	91 (82.0)	
Hb	14.2 ± 8.0	15.0 ± 13.5	13.6 ± 2.2	13.9 ± 2.8	0.638
PLT	271.3 ± 133.2	243.6 ± 100.4^B	314.6 ± 131.6^A	262.2 ± 152.1^{AB}	**0.026**
WBC	13.9 ± 7.3	13.3 ± 6.8	15.5 ± 9.8	13.4 ± 6.1	0.190
ESR	58.8 ± 29.1	55.3 ± 30.5	60.5 ± 29.0	60.5 ± 28.2	0.562
RBG	269.5 ± 179.4	109.1 ± 23.7^C	167.6 ± 19.0^B	391.6 ± 170.6^A	**<0.001**
ALT	54.9 ± 47.8	44.9 ± 37.1	64.5 ± 61.0	52.9 ± 37.1	0.103
AST	41.9 ± 22.0	40.7 ± 20.2	43.4 ± 19.2	41.0 ± 25.2	0.799
ALP	98.8 ± 70.9	90.4 ± 39.6^{AB}	84.3 ± 59.4^B	116.1 ± 92.8^A	**0.041**
CHOL	181.2 ± 87.2	165.5 ± 61.0	180.0 ± 93.4	192.9 ± 100.1	0.243
TRIG	200.3 ± 118.9	189.7 ± 119.9	211.2 ± 119.7	198.6 ± 118.3	0.676
SCr	1.7 ± 5.4	1.7 ± 5.5	1.1 ± 0.7	2.0 ± 7.0	0.670
BUN	63.7 ± 66.3	54.0 ± 31.9	59.1 ± 42.8	75.1 ± 94.9	0.205

Values are given as either mean $\pm$ standard deviation or a number followed by a percentage in parentheses

Rh: Rhesus blood group; Hb: Hemoglobin (g/dL); PLT: Platelets (10^9/L); WBC: White blood cell (10^9/L); ESR: Erythrocyte sedimentation rate (mm/hour); RBG: Random blood glucose (mg/dL); ALT: Alanine aminotransferase (U/L); AST: Aspartate aminotransferase (U/L); ALP: Alkaline phosphatase (U/L); CHOL: Total serum cholesterol (mg/dL); TRIG: Triglycerides (mg/dL); SCr: Serum creatinine (mg/dL); BUN: Blood urea nitrogen (mg/dL); *p*: Person Chi-square test or one-way analysis of variance probability followed by Duncan multiple range test post hoc (Significant *p*-value is marked in bold). Different superscript letters indicate significant difference between means in rows ($p \leq 0.05$), while similar letters indicate no significant difference ($p > 0.05$)

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Fig. 1 Scatter dot plot of random blood glucose in COVID-19 patients with normoglycemia (109.1 ± 23.7 mg/dL), prediabetes (167.6 ± 19.0 mg/dL) or diabetes (391.6 ± 170.6 mg/dL). Mean and standard deviations are indicated by horizontal and vertical lines respectively

22.5% prediabetes and 52.1% diabetes. Thus, the role of COVID-19 in the development of diabetes was proposed. Consistent with our observation, it has been reported that hyperglycemia occurred in 33.2% of COVID-19 patients during hospitalization, and the proportion was higher in severe cases compared to nonsevere cases (45.4 vs. 21.5%) [5]. Accordingly, it has been hypothesized that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may reduce insulin secretion through its effects on pancreatic β-cell function [7, 8]. The SARS-CoV-2 receptor (ACE2: angiotensin-converting enzyme 2) has been shown to be expressed by pancreatic cells, as well as other metabolic organs and tissues (for instance, adipose tissue, intestine and kidneys). Therefore, the virus may cause multidirectional changes in glucose metabolism that could complicate pre-existing diabetes or lead to the development of hyperglycemia in non-diabetic patients [9]. Furthermore, it has also been demonstrated that COVID-19 patients are markedly characterized by elevated serum levels of pro-inflammatory cytokines; for instance, interleukin (IL)-1, IL-6, IL-12, interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α) [10, 11]. Inflammation due to high production of cytokines may lead to insulin resistance and may impair insulin production by pancreatic β-cell [8].

Equally important, most current COVID-19 patients were overweight/obese (79.8%), and there has been strong evidence to suggest that obesity is involved in the pathogenesis of diabetes [12]. More importantly, a global estimate revealed that 45.8% of all adult diabetes cases were undiagnosed, and almost a similar proportion was reported in Iraq (47.05%) [13]. Therefore, although the patients of this study did not have a clinical history of diabetes, they may represent undiagnosed cases especially if we consider their overweight/obese status. Taken together, these data suggest that diabetes may be considered a risk factor for COVID-19, or the infection may put non-diabetic patients at risk for developing diabetes. However, additional prospective studies are warranted to understand the pathophysiology of COVID-19 in diabetic and non-diabetic patients, and to limit confounding biases due to observational design [14].

Declarations

Ethics approval and consent to participate
The Ethics Committee at the Iraqi Ministry of Health and Environment approved the study (Approval number: 68130 on 10/11/2020).

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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