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Research Article

Incidence of Glucose Dysregulation in Patients with COVID-19 in Babylon Governorate, Iraq

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A B S T R A C T

Introduction: COVID-19 is a novel illness caused by an RNA Coronavirus. Diabetes was a risk factor for poor outcomes in the previous SARS-1 and Middle East Respiratory Syndrome (MERS) and is considered now an independent risk factor for poor outcomes in cases of SARS-2 (COVID-19). A number of studies referred to the association between COVID infection and impaired glycaemic state.

Aims: To find the incidence of dysglycaemia in COVID-19 patientsand assess characteristics that put the patients at higher riskof it.

Method: A total of 148 patientsadmitted between JuneandSeptember 2020 with a diagnosis of COVID-19 were included, anddivided into 3 glycaemic groups.

Results: In 148 patients diagnosed with COVID 19, dysglycaemiawas disclosed in 55.4% with frank new-onset diabetes in more than half of them (56%).Younger aged patients, those with higherweight, and longer disease duration were at higher risk.Further, the mean lung involvement presented by CT scan was higher in those with dysglycaemia.

Conclusion: More than 50% of COVID patients developed dysglycaemia for the first time. Young age, high weight, and long disease duration were significant risk factors.

Keywords: Incidence, Glucose Dysregulation, COVID-19

Introduction

Coronavirus disease 2019 (COVID-19) is a novel illness caused by an RNA Coronavirus. It has been spreading widely throughout the globe and has been associated with high fatalities and complications. Diabetes is a growing problem internationally with many complications that can be life-threatening. Diabetes was a risk factor for poor outcomes in the previous SARS-1 and Middle East Respiratory Syndrome (MERS). Since the declaration of COVID-19 as a pandemic in early 2020, many studies have been conducted on the relationship between diabetes and COVID-19. These studies showed that diabetes is an independent risk factor for poor outcomes in patients infected with the novel virus.[1]Diabetes and hyperglycaemic states are associated with poor outcomes in patients with COVID-19, including the rates of hospital admission, the need for assisted ventilation and even mortality. This is mainly because diabetes and high glucose readings are associated with impaired host's

humoral and innate immune system. Moreover, diabetes is associated with the release of inflammatory mediators especially interleukin 6 (IL-6) which is implicated in the cytokine storm. Finally, diabetes is associated with the reduction of lung vital capacity and can lead to alveolar dysfunction.[2,3] On the other hand, SARS-2 infection (COVID-19) is associated with deterioration of the glycaemic profiles in patients with diabetes. Moreover, COVID-19 has been associated with new-onset diabetes and states of hyperglycaemia that would not be classified as diabetes (impaired fasting glucose and impaired glucose tolerance). Some of these cases present with severe ketoacidosis and/ or hyperosmolar states that need high doses of insulin to treat.[4] COVID-19 can cause these new dysglycaemic events by multiple mechanisms: first, viral infection has a well-establishedimpact on the pancreatic cells and there is a causal relationship between different viruses (such as Epstein Barr viruses,Coxsackie-viruses and Enteroviruses) and type 1 diabetes. Similarly, type 2 diabetes has been linked to cases of hepatitis Cviruses. Second,COVID-19 can trigger states of dysglycaemia as a stress response associated with severe illness. Third, SARS-CoV-2 virus that causes COVID-19binds to angiotensin-converting enzyme 2 (ACE2) receptors, which are expressed heavily in the pancreatic beta cells.[12] Fourth, steroids use in the treatment course of COVID-19 is associated with the occurrence of "new diabetes", or secondary diabetes. Thus, it has been postulated that SARS-CoV-2 may cause alterations of glucose metabolism that could worsenpreexisting diabetes or lead to new onset of glycaemic dysregulation in these patients.[4,5]

Aims

To snap the incidence of dysglycaemic states in patients with COVID-19 and assess the characteristics that put the patients at higher risk to develop dysglycaemia.

Method

148 patients were included in the study who had been admitted with the diagnosis of COVID by positive PCRand or chest CT during the period from June to September 2020. Following patients were included:

- No history of diabetes before; not received steroid or any treatment before; andagreed to participate in the study

Divided into 3 groups according to the ADA definition criteria as:

- New-onset diabetic as fasting blood glucose >126 mg/ dL, or 2 hours postprandial blood glucose >200 mg/ dL, or/ and HbA1c > 6.5
- Impaired glucose tolerance tests: fasting blood glucose level 100-125 mg/dL, or 2 hours postprandial 150-199 mg/dL, or HbA1c 5.7-6.4
- Normal: below the above figures

The data taken from patients included:

- Gender: male & female
- Family history: patient with 1st-degree relatives with diabetes labelled as +ve family history(in father, mother, sons, brother or sisters)
- Duration: the duration in days from the onset of symptoms to the evaluation
- The presentation: classic for DM (polyuria,polydipsia, dry mouth) versus other as asymptomatic or fatigue
- Examinations were done concentrating on weight, respiratory rate & SPO_2
- CRP & CBD concentrating on the absolute lymphocytes count by autolyzer machine

Results

148 COVID-19 patients were eligible to be involved in the study. Testing their glycaemic profiles revealed that 46 patients have developed new-onset diabetes and 36 patients have developed impaired glucose tolerance tests. So those with dysglycaemic states (abnormal glucose level profiles) represented 55.4% of the study sample and those with frank new diabetes accounted for 56%, as presented in Figure 1.

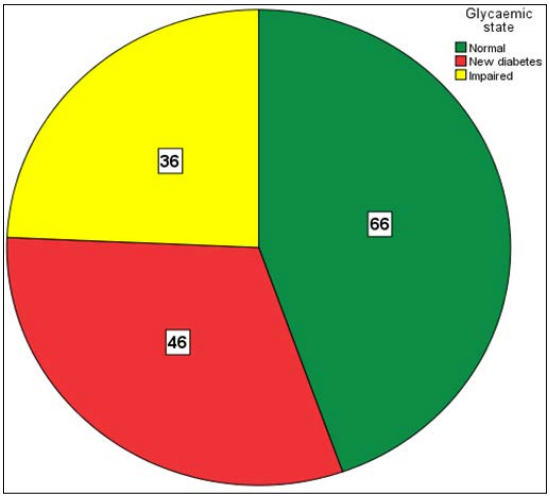

Figure 1.Percentages of Glycaemic States in Patients with COVID-19

Studying history characteristics of those patients have shown thatpatients with young age, positive family history of diabetes and with longer disease duration are at higher risk of developing dysglycaemia. In contrast, gender has not shown any measurable effect on the glycaemic profiles as shown in Table 1.

By examining the patients' physical characteristics, only higher body weight appeared to be significantly associated with developing abnormal glycaemic profiles. On the other hand, neither rapid respiratory rate nor low SPO_2 appeared to be affecting the glycaemic profile of the patients significantly as shown in Table 2.

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Table 1.Association between History Characteristics and Development of Dysglycaemiain Patientswith COVID-19

	Glycaemic State	Normal N (%)	Impaired or Diabetic N (%)	Total N (%)	P value
Age group (years)	18-35	0 (0.0)	7 (100)	7(4.73)	0.03
	36-50	21(52.5)	19 (47.5)	40 (27.02)	
	Over 50	45 (44.6)	56 (55.4)	101(68.2)	
Gender	Male	36 (50.7)	35 (49.3)	71 (48)	0.151
	Female	30 (39.0)	47 (61.0)	77 (52)	
Family Hx	Positive	15 (27.8)	39 (72.2)	54 (36.5)	0.002
	Negative	51 (54.3)	43 (45.7)	94 (63.5)	
Duration	Less than 14 ds	65 (60.2)	43 (39.8)	108 (72.97)	0.0001
	14+	1 (2.5)	39 (97.5)	40 (26.03)	

Table 2.Association between COVID-19 Patients' Physical Characteristics and the Development of DysglycaemiaStates

	Glycaemic state	N	Mean	Standard Deviation	P value
Respiratory rate	Normal	66	21.56	4.59	0.136
	Impaired or diabetic	82	22.65	4.29	
SPO_2	Normal	66	87.56	3.34	0.315
	Impaired or diabetic	82	86.34	9.35	
Body weight	Normal	66	70.272	11.21	0.003
	Impaired or diabetic	82	88.195	47.83	

Table 3.Association of Blood Parameters with Glycaemic state in COVID-19 Patients

	Glycaemic State	N	Mean	Standard Deviation	P value
Lymphocytes count	Normal	66	1117.81	398.61	0.0001
	Impaired or diabetic	82	894.48	353.18	
CRP	Normal	66	1.045	0.209	0.484
	Impaired or diabetic	82	1.024	0.155	
CT	Normal	66	60.09	11.276	0.001
	Impaired or diabetic	82	67.56	13.77	

Laboratory investigations in COVID-19 patients have shown a significant association between diminished lymphocyte count and the development of dysglycaemic states. Similarly, there was a significant correlation between the more disseminated lung involvement by the CT scan and the rates of dysglycaemia (the higher the percentage of lung destruction shown by CT scan the more the rate of dysglycaemia). Yet, patients' inflammatory marker CRP failed to show a significant correlation with the abnormal glycaemic profiles. These findings are illustrated in Table 3.

Discussion

Since the declaration of COVID-19 as a pandemic in early 2020, many studies have been conducted on the relationship between COVID-19 and diabetes. Besides diabetes has been proved as an independent risk factor for poor outcomes in COVID-19 patients, SARS-2 virus has been associated with deterioration of the glycaemic profiles in patients with diabetes, which reflects a bidirectional relationship between the two pandemics (diabetes and COVID-19).[1-5,13,19] Moreover, states of new-onset dysglycaemia (diabetes and impaired glucose tolerance) were not uncommon to be observed in patients with COVID-19.[6-8,10,11,18] Our current study is a prospective observational study that was carried out in Merjan Teaching Hospital, in Babylon Governorate, Iraq. This study has included 148 patients who were proved to have COVID-19 by PCR and chest CT scan. The study showed that 46 patients have developed new-

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onset diabetes (according to the ADA definition criteria: fasting blood glucose >126 mg/dL, or 2 hours' postprandial blood glucose >200 mg/dL, or/ and HbA1c > 6.5). Also, our study has shown that 36 patients have developed impaired glucose tolerance tests (according to the ADA definition criteria: fasting blood glucose level 100-125 mg/dL, or 2 hours postprandial 150-199 mg/dL, or HbA1c 5.7-6.4). This means that more than 55% of our sample size have developed new dysglycaemic events as shown in Figure 1. This result was like the result of a small study in the United States conducted by Bhatraju et al. who reported diabetes to be associated with 58.0% of the patients with COVID-19. Another study in Italy has shown that 34% of the patients with COVID-19 had diabetes.[2] It should be noted here that these findings could reflect the high prevalence of diabetes across the globe and especially in our country. Similarly, Zhang et al. have shown in their retrospective study that new-onset diabetes represents 16% of their COVID-19 cases (26/166).[9] Li J et al. have reported 21% of COVID-19 patients had new-onset diabetes (94/435). Wang et al. have reported 29% of their cases had new-onset diabetes (176/605).[1,2,9] Surprisingly, our study has shown that younger age is a risk factor to develop abnormal glycaemic profiles and this might be due to our small sample size. In addition, the current study shows that positive family history for diabetes is an important risk factor to develop dysglycaemia, and this agrees with the eminent fact that the percentage of diabetes among individuals who have a first-degree relative with diabetes is significantly higher than that of individuals without a family history.[10] Also,patients with a longer duration of COVID-19 tend to have a higher risk to develop abnormal glycaemic profiles as they encounter a more protracted disease course, and they areexposed to much inflammatory stress, and perhaps due to the prolonged use of steroids.[11] The study has also shown that gender did not affect the risk of dysglycaemia significantly. All these findings are illustrated in Table 1. Furthermore, our study showed that patients with high body weight are at a significant risk to develop dysglycaemia, as high body weight is associated with more insulin resistance.[10,15,16] In contrast, low oxygen saturation and high respiratory rate have not influenced the dysglycaemic risk significantly, as shown in Table 2. Patients' abnormal inflammatory markers (lymphocyte count but not the C reactive protein) have a significant impact on the patients' glycaemic profiles, as they can reflect the severity of the COVID-19, and this was similar to the results of other studies that showed the effect of inflammatory markers in the pathogenesis of new-onset dysglycaemia in COVID-19 patients.[14,17] Similarly, the degree of pulmonary involvement by COVID-19 on the imaging study (CT scan) has a significant impact on the patients' glycaemic states; as much as the lung destruction by the CT scan as much as the risk to develop dysglycaemia in COVID-19 patients.

Conclusion

This study shows that more than 50% of the COVID-19 patients have developed new-onset dysglycaemic states (new-onset diabetes and impaired glucose tolerance states). Young age, high body weight, and long disease duration were significant risk factors to get abnormal glycaemic profiles. Also, diminished lymphocytic count and diffuse lung involvement as shown by chest CT scan influence the rates of dysglycaemia.

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Conflict of Interest: None

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