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Research Article

Prevalence of Glucose Intolerance and New-Onset Diabetes in COVID-19 Infected Patients in Babylon Province, Iraq

Iman Shaker Abd Al-Zahra[1], Nihad Abdallah Selman[2]

[1]Babylon Health Director, Babylon, Iraq.
[2]Assistant Professor, College of Medicine, University of Babylon, Endocrinologist.
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I N F O

Corresponding Author:
Nihad Abdallah Selman, College of Medicine, University of Babylon, Endocrinologist.
E-mail Id:
dr.nihad2005@uobabylon.edu.iq
Orcid Id:

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A B S T R A C T

Background: The pathology of COVID-19 was found to go beyond acute respiratory infection. Hyper-inflammatory syndrome had described among some patients. Many persons with COVID-19 who require hospitalization also have diabetes, according to studies.

Objectives: To identify the prevalence of glucose intolerance and newly diagnosed diabetes in COVID-19 infected patients and its correlation with disease severity and drugs used.

Methodology: A cross-sectional study was conducted in Marjan Medical City during April-July 2021. The study included 355 patients not previously diagnosed with diabetes who were admitted to the hospital for COVID-19 infection.

Results: Mean age of participants was (48.12 ± 15.51) years, with females constituting the larger proportion (53.52%). Newly diagnosed diabetic patients formed (15.77%) while pre-diabetic patients formed (22.82%). The use of certain medications was found to be significantly related to diabetes status, including Favipiravir and Remdesivir. Lung involvement was found to be significantly higher among diabetic (42.3% ± 17.2%) and pre-diabetics (40.1% ± 13.0%) compared to non-diabetics (35.0% ± 14.8%).

Conclusion: Approximately (39%) of the patients with COVID-19 in various age groups had pre-diabetes status or newly diagnosed diabetes that was not diagnosed. Those patients had a significantly higher level of lung involvement compared to non-diabetic patients.

Keywords: Prevalence, Glucose Intolerance, New-onset Diabetes, Babylon Province

Introduction

In December 2019, a novel coronavirus, SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), produced an outbreak of pneumonia in Wuhan City, Hubei Province, China, and the sickness was dubbed coronavirus disease 2019 (COVID-19).[1] Researchers have identified two new illness periods linked with SARS-coronavirus-2 infection,

including an uncommon hyper-inflammatory condition after an acute period and late inflammatory and virological consequences, based on the available data. These three disease periods reflect not only the time course of SARS-CoV-2 infection at the population level, but also the likely involvement of several organs, including diabetes mellitus.[2] Many persons with COVID-19 who require hospitalisation also have diabetes, according to studies. For example, 85.9% of 184 patients hospitalized to a New Jersey hospital for COVID-19 had diabetes mellitus (62.0 per cent, HbA1c 6.5 per cent) or prediabetes (23.9 per cent, HbA1c = 5.7-6.4 per cent), according to a recently published study. A further 4.3 per cent of individuals had a normal HbA1c but a BMI of more than 30 kilograms per meter squared.[3] Diabetes is 4.7 times more common in this patient group than in the general population of the United States, while prediabetes is 1.3 to 6.4 times more common. A large majority of the patients were clinically obese, with a BMI of more than 30 kg/m.[2] Although diabetics and non-diabetics are both likely to expose to COVID-19, diabetics are more likely to have poor outcomes and require hospitalization due to some element of diabetes.[3] Diabetes is widespread among people admitted to hospitals with coronavirus disease 2019 (COVID19), and it's linked to a higher risk of death.[4] Stress-induced hyperglycemia, which occurs during hospitalization for an acute medical or surgical illness in people who have never had diabetes, is a worse predictor of poor clinical outcomes and mortality than diabetes. At admission, hyperglycaemia was an independent predictor of mortality in patients with severe acute respiratory syndrome.[5] COVID-19 and diabetes are linked in a bidirectional manner. Diabetes, on the one hand, is linked to a higher incidence of severe COVID-19. In patients taking Covid-19, however, new-onset diabetes and severe metabolic consequences of preexisting diabetes, such as diabetic ketoacidosis and hyperosmolarity, necessitating extremely high insulin doses, have been reported. These diabetic symptoms are difficult to control in the clinic and reflect a complicated aetiology of COVID-19-related diabetes. The virus that causes COVID-19, the severe acute respiratory syndrome coronavirus (SARS-CoV-2), binds to angiotensin-converting enzyme 2 (ACE2) receptors, which are expressed in critical metabolic organs and tissues such as pancreatic beta cells, adipose tissue, the small intestine, and the kidneys.[6] As a result, it's possible that SARS-CoV-2 causes pleiotropic changes in glucose metabolism, which could exacerbate the pathophysiology of pre-existing diabetes or lead to new disease processes. Other coronaviruses that bind to ACE2 receptors have also been implicated in the development of ketosis-prone diabetes.[6] Patients with SARS coronavirus pneumonia have been found to have higher rates of fasting hyperglycemia and acute onset diabetes than those with non-SARS pneumonia. Overall, these findings support the concept that COVID-19 may have a diabetogenic effect in addition to the well-known stress response associated with severe illness.[6]

Objectives

The objectives of the study were to find the prevalence of glucose intolerance and newly diagnosed diabetes in COVID-19 infected patients and its correlation with disease severity and drugs used.

Methods

This is a cross-sectional study which is conducted on 355 patients at Marjan Medical City from 1st of April to 1st of July 2021. Data is collected by using a pre-designed questionnaire format for purpose of the study to be interviewed after giving their verbal consent. Each patient was interviewed for about 10 minutes. The questionnaire includes; name, age, gender, height, weight, BMI, family history of DM, history of hypertension, BP, smoking and in females, history of PCOS or gestational DM. Investigations that conducted to all patients are: (FBS, RBS, blood urea -by spectrophotometer-) at time of admission, PCR test for COVID 19, CT scan (the percentage of lung involvement estimated by specialist radiologist), O_2 saturation; by oximeter. Type of drugs used during hospitalization. Measurement of SpO_2 was performed using a pulse oximeter. Height and weight were measured using tape-measure and weighing devices in the ward, respectively. BMI was calculated according to the formula:

$$BMI = \frac{\text{Weight (in kg)}}{\text{Height (in meters)}^2}$$

Inclusion Criteria

All patients visiting Marjan teaching hospital with positive PCR for COVID-19 with newly diagnosed diabetes.

Exclusion Criteria

- Any patient with a previous history of hyperglycaemia or diabetes.
- Patients with -ve PCR whose diagnosis with COVID-19 was established according to CT findings.

A study protocol was reviewed and granted permission by the Ethical Committee of Babylon University, College of Medicine. After explaining the objectives of the study to the patients, verbal consent was obtained from them prior to interviewing. The statistical analysis for this study was performed using SPSS® software (version 23.0 for Linux® operating system). Categorical variables were expressed as frequencies and percentages, whereas continuous variables were represented as means and SD. The ANOVA test was used to compare means between three or more groups, whereas the Student's t-test was used to compare means between two groups. The association between

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categorical variables was evaluated using the Chi-square test. A statistically significant P-value of less than 0.05 was used.

Results

This study included a total of 355 patients, age of participants ranged from 13 years to 95 years with a mean age of (48.12 ± 15.51) years. Table 1 provides details of the general characteristics of the patients.

Table 1.General Characteristics of Patients

Characteristics		Mean ± SD or N (%)
Total number of patients		355
Gender	Male	165 (46.5%)
	Females	190 (53.5%)
Mean age		48.12 ± 15.51 years
Mean height		167.23 ± 9.17
Mean weight		79.28 ± 13.06
Mean BMI		28.52 ± 3.75
Mean blood urea		8.33 ± 11.10
Mean blood pressure	Systolic	124.48 ± 13.67
	Diastolic	79.22 ± 9.40
Smoking	Yes	82 (23.10%)
	No	273 (76.90%)
Mean lung involvement		37.54% ± 14.53%
Mean SPO_2		93.29% ± 4.51%

Females comprised the larger proportion of study participants (53.52%), vs (46.48%) males. Mean age of male patients was 47.68 ± 15.55 years, while mean age of female patients was 48.49 ± 15.51 years. No significant difference in age was observed between males and females, t-test = 0.49, p value = 0.627. Mean BMI of study participants was 28.28 ± 3.99 kg/m^2. The majority of study participants (56.6%) were overweight (BMI between 25.0 and 29.9 kg/m^2). Mean systolic blood pressure of study participants was 124.47 ± 13.67 mmHg, while mean diastolic blood pressure of study participants was 79.22 ± 9.40 mmHg. Mean proportion of lung involvement among patients was 37.54% ± 14.53%, while mean O_2 saturation was 93.29% ± 4.51%. Patients who were non-diabetic (RBS < 7.78 mmol/L) were 218, forming 61.41% of the total patients, while patients who were found to be prediabetic (RBS: 7.78-11.06 mmol/L) were 81, forming 22.82% of the total study patients. Patients who were found to be diabetic (with RBS > 11.06) were 56, forming 15.77% of the total patients. These findings have been illustrated in Figure 1.

Comparison between the group of patients (non-diabetics, pre-diabetics, and diabetics) and BMI was performed using Chi-square test. No significant relationship was observed between diabetes status and BMI (p value = 0.117). Similarly, no significant relationship was observed between diabetes status and gender (p value = 0.825). Regarding past medical history, there was a significant relationship between diabetes status and history of hypertension (HT) (p value < 0.001). Proportion of hypertensive patients who were diabetic or pre-diabetic was significantly larger than the proportion of non-hypertensive patients with diabetes or pre-diabetes. In a similar manner, there was a significant relationship between diabetes status and history of smoking (p value = 0.041). History of PCOS among females was also found to have a significant relationship with diabetes status (p value = 0.005). No significant relationship was found between diabetes status and family history of DM. Details are provided in Table 2.

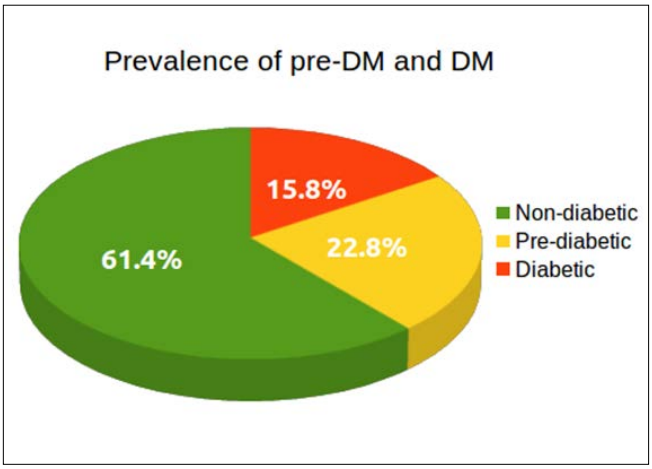

Figure 1.Proportion of Newly Diagnosed Diabetic Patients among Study Participants (n = 355)

Chi-square test was used to assess the relationship between diabetes status and certain medications. There was a significant relationship between diabetes status and use of Favipiravir (p value = 0.009) (Table 3). Similarly, there was a significant relationship between diabetes status and use of Remdesivir (p value = 0.038) (Table 3).

There was also a significant relationship between the daily dose of decadrone and the status of diabetes (p value = 0.032) (Table 4).

For other medications, there was no significant relationship between diabetes status and each of Ceftriaxone, Azithromycin, Vancomycin, Garamycin, Heparin/ Enoxaparin, or herbal medications (p value = 0.293, 0.288, 0.163. 0.646, 0.564, and 0.271, respectively). Details are provided in Table 5.

Regarding the severity of disease, ANOVA test had revealed that there is a significant difference in mean lung involvement among the three study groups (non-diabetics, pre-diabetics, and diabetics) (ANOVA f value = 7.36, p value = 0.001) (Table 6).

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Table 2.Past Medical History of Study Participants

Past Medical History		Diabetes Status			Total N (%)	P value
		Non-diabetic N (%)	Pre-diabetic N (%)	Diabetic N (%)		
HT	Yes	33 (50.00)	27 (40.91)	6 (9.09)	66 (100)	< 0.001*
	No	185 (64.01)	54 (18.69)	50 (17.30)	289 (100)	
Smoking	Yes	45 (54.88)	27 (32.93)	10 (12.20)	82 (100)	0.041*
	No	173 (63.37)	54 (19.78)	46 (16.85)	273 (100)	
PCOS[F]	Yes	-	3 (100)	-	3 (100)	0.005*
	No	119 (62.63)	40 (21.39)	28 (14.97)	187 (100)	
Family history of DM	Yes	30 (54.55)	19 (34.55)	6 (10.91)	55 (100)	0.067
	No	188 (62.67)	62 (20.67)	50 (16.67)	300 (100)	

* Significant at p ≤ 0.05; [F] Calculated among 190 female patients.

Table 3.Favipiravir & Remdesivir Use among Study Participants

Diabetes status	Favipiravir Use			P value
	Yes N (%)	No N (%)	Total N (%)	
Non-diabetic	46 (21.10)	172 (78.90)	218 (100)	0.009*
Pre-diabetic	7 (8.64)	74 (91.36)	81 (100)	
Diabetic	5 (8.93)	51 (91.07)	56 (100)	
Total	58 (16.34)	297 (83.66)	355 (100)	
Diabetes status	**Remdesivir use**			**P value**
	Yes N (%)	No N (%)	Total N (%)	
Non-diabetic	160 (73.39)	58 (26.61)	218 (100)	0.038*
Pre-diabetic	70 (86.42)	11 (13.58)	81 (100)	
Diabetic	46 (82.14)	10 (17.86)	56 (100)	
Total	276 (77.75)	79 (22.25)	355 (100)	

* Significant at P ≤ 0.05.

Table 4.Decadrone Use among Study Participants

Decadrone Dose Per Day	Diabetes Status			Total	P value
	Non-diabetic N (%)	Pre-diabetic N (%)	Diabetic N (%)		
None	1 (33.33)	-	2 (66.67)	3 (100)	0.032*
1	158 (62.20)	64 (25.20)	32 (12.60)	254 (100)	
2	57 (59.38)	17 (17.71)	22 (22.92)	96 (100)	
3	2 (100)	-	-	2 (100)	
Total	218 (61.41)	81 (22.82)	56 (15.77)	355 (100)	

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Table 5.Other Medications Used by Study Participants

Medications	Diabetes Status			Total (n = 355) N (%)	P value
	Non-diabetic (n = 218) N (%)	Pre-diabetic (n = 81) N (%)	Diabetic (n = 56) N (%)		
Ceftriaxone	87 (39.91)	30 (37.04)	16 (28.57)	133 (37.46)	0.293
Azithromycin	5 (2.29)	-	2 (3.57)	7 (1.97)	0.288
Vancomycin	76 (34.86)	33 (40.74)	27 (48.21)	136 (38.31)	0.163
Garamycin	48 (22.02)	22 (27.16)	13 (23.21)	83 (23.38)	0.646
Heparin/ Enoxaparin	178 (81.65)	68 (83.95)	43 (76.79)	289 (81.41)	0.564
Herbal medications	4 (1.83)	-	2 (3.57)	6 (1.69)	0.271

* Significant at P ≤ 0.05.

Table 6.Comparison of Lung Involvement among Study Groups

Group	N	Mean ± SD	Range	P value
Non-diabetic	218	35.00 ± 14.76	5.00-75.00	0.001*
Pre-diabetic	81	40.12 ± 12.98	10.00-75.00	
Diabetic	56	42.33 ± 17.17	10.00-85.00	
Total	355	37.32 ± 15.05	5.00-85.00	

Comparison	Mean difference	P value
Non-diabetic vs pre-diabetic	5.13	0.008*
Non-diabetic vs diabetic	7.33	0.001*
Pre-diabetic vs diabetic	2.21	0.391

* Significant at P ≤ 0.05.

Discussion

The correlation between diabetes and increased body weight (whether being overweight or obese) had been described for both type I and type II diabetes.[7] The majority of study participants in the present study had abnormal BMI. More than (50%) of them were either overweight or obese. This finding probably reflects the demographic characteristics of the Iraqi population. The study by Pengpid S et al. estimated that more than (65%) of the Iraqi people were either overweight or obese.[8] Another study conducted in Erbil and published in 2019 had reported that (41%) of the population were obese while (33%) were overweight, forming more than (70%) combined.[9] The present study had demonstrated that (15.77%) of the patients had undiagnosed diabetes. This proportion is similar to the proportion of (15.8%) reported by Vargas-Vazquez A et al. in their study conducted in Mexico in 2020, which included 317 patients.[10] Various studies had reported different proportions of undiagnosed diabetes among COVID-19 patients. Li H et al. had reported a proportion of (20.75%) of patients with newly diagnosed diabetes in their study that included (453) patients[11], while the study by Tee L et al. had reported a smaller proportion of only (5.8%) in their study that included 240 patients.[12] However, a systemic review by Sathish T et al. had reported a pooled proportion of (14.4%)[13], which is closely similar to the proportion of (15.77%) described by the present study. The relationship between diabetes and COVID-19 had been described as "bidirectional". In one direction, diabetes can lead to more severe COVID-19 disease, while in the other direction, some patients with COVID-19 are observed to develop new-onset diabetes as well as severe metabolic complications of already-diagnosed diabetes.[14,15] Pre-diabetic patients in the present study formed a proportion of 22.82% of the study sample. The study by Smith S et al. conducted in New Jersey/ USA on (184) hospitalized patients for COVID-19 had reported that pre-diabetics formed a proportion of (23.9%)[16], which is closely similar to the finding in the present study. Other studies had reported different findings. Vargas-Vazquez A et al. had demonstrated a higher proportion of (39.4%) in their study[10], while Tee et al. demonstrated a lower proportion of only (8.8%).[12] Pre-diabetes status had been proposed to be one of the comorbidities for COVID-19, with its possible influence on the clinical course of the disease and its fatality.[17] It has been described that certain inflammatory cytokines can be elevated due to the pre-

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diabetic state, particularly regarding C-reactive protein (CRP), interleukin-6 (IL-6), and tumour necrosis factor alpha (TNF-α), with changes in the concentrations of immune cells; reflecting an immune activation.[18] The present study had shown that Favipiravir use was significantly higher among non-diabetic patients (21.10%) compared to pre-diabetic patients (8.64%) and diabetic patients (8.93%). In contrast, the use of Remdesivir was significantly lower among non-diabetic patients (73.39%) compared with pre-diabetic patients (86.42%) and diabetic patients (82.14%). The study by Qureshi Q et al. had demonstrated that remdesivir is effective in the treatment of both non-diabetic patients and diabetic patients. However, they indicated that remdesivir had shown significantly more delay in recovery among diabetic patients compared with non-diabetic patients.[19] Lung involvement was found to be significantly higher among diabetic and pre-diabetic patients compared to non-diabetic patients. Oliveira T et al. had suggested that the proliferation of SARS-CoV-2 is affected by glucose metabolism in both type 1 and type 2 cells. This, combined with the close relationship between pathways of glucose metabolism in the lung and the pro-thrombotic and inflammatory responses; may result in severe consequences.[20]

Conclusion

This study concluded that 137 patients (38.59%) with COVID-19 in various age groups had dysglycemia (22.8% pre-diabetes status & 15.8% diabetes that was not diagnosed as diabetes before seeking healthcare for COVID-19). Patients with diabetes and pre-diabetes were found to have significantly more severe disease, as indicated by the significantly higher level of lung involvement among patients with diabetes or pre-diabetes compared to those who are non-diabetic.

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Conflict of Interest: None

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