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Effects of Covid-19 Infection on Some Pancreatic Functions in Diabetic Patients at Thi-Qar Province/Iraq

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***Abstract*: People with diabetes mellitus (DM) represent a population group that is at high risk of developing a poor prognosis for COVID-19.Having diabetes can lead to serious illness, ICU stay, and death from COVID-19.The current study included 150 participants with diabetes, 100 of whom had COVID-19 (46 males, 54 females), and 50 had diabetes only (28 males and 22 females), aged between 37 and 69 years. The current situation is in the isolation center for people infected with the Corona virus at Al-Hussein Teaching Hospital and Shatrah General Hospital in Thi-Qar Governorate.The study included the impact of COVID-19 infection and its effect on pancreatic function.The results of the current study recorded a significant increase in fasting blood glucose concentration and cumulative glucose concentration in diabetic patients infected with Covid-19 virus compared to diabetic patients only by gender, the results also indicated an increase in fasting glucose and cumulative glucose levels in both male and female COVID patients compared to only diabetic patients. The concentration of pancreatic hormones also increased significantly in both male and female patients infected with Covid-19 virus compared to diabetic patients. According to age groups and BMI, cumulative and fasting glucose concentrations did not register a significant difference according to age groups, while according to BMI, cumulative and fasting glucose concentrations increased in patients with normal weight. Trypsin concentration increased significantly in the first age group, while glucagon increased in the second age group. Trypsin and glucagon did not score a significant difference according to BMI**

***Keywords*: : Diabetic, Covid-19, Pancreas**

I. INTRODUCTION

Coronaviruses are a broad group of viruses that infect a wide range of animals, as well as people, and can cause moderate to severe respiratory illnesses. Two highly pathogenic zoonotic coronaviruses, severe acute respiratory syndrome coronavirus (SARS-COV) and Middle East respiratory syndrome coronavirus (MERS-COV), caused fatal respiratory illness in humans in 2002 and 2012, respectively, making emerging coronaviruses a new public health concern in the twenty-first century (Hu *et al.*, 2021).COVID-I9 symptoms vary, ranging between mild and severe diseases. Headache, loss of taste and

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smell, nasal congestion and rhinorrhea, cough, pain in the muscle, sore throat, fever, and breathing problems are common symptoms (Habeeb and Hussain, 2021)

Non gastrointestinal symptoms of COVID-19 include fever, cough, shortness of breath, chills, repeated shaking with chills, muscle pain, headache, sore throat, and new loss of taste or smell. Gastrointestinal (GI) symptoms, including anorexia, nausea, vomiting, abdominal pain, and/ or diarrhea have been reported in patients with COVID-19. Additionally, abnormal liver enzymes are also observed (Sultan *et al.*, 2020). It is known that diabetic patients, especially those with uncontrolled glycemia, are at higher risk to contract infections, a trend that correlates tightly with glycated hemoglobin levels. In clinical practice, higher incidence of foot infections, yeast infections, urinary tract infections, and surgical site infections is commonly seen in diabetic patients (Mazucanti and Egan, 2020). It has been stated that COVID-19 is associated with hyperglycemia, actually considered a direct predictor of the poor prognosis of the disease and an increased risk of death, briefly, the binding site and entry point of SARS-CoV-2 is the ACE2 receptor, which is highly expressed in the lung, liver, brain, placenta, and pancreas.SARS-CoV-2 infects the pancreas through ACE2, being highly expressed there when compared to other organs, leading to pancreatic damage with subsequent impairment of insulin secretion and development of hyperglycemia even in non-DM patients. Similarly, SARS- CoV-2-induced pancreatic injury may worsen a preexistent DM (Al-kuraishy *et al.*, 2021). Coronavirus disease 2019 (COVID-19) is an ongoing pandemic infection caused by the positive-sense RNA virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Although initial studies focused on lung injury and cardiovascular manifestations, other organ dysfunctions have been observed, notably in the kidney, pancreas, intestine, and olfactory epithelia (Gheblawi *et al.*, 2020). The GI manifestations of the COVID-19 infection include anorexia, nausea, vomiting, abdominal pain, and diarrhea. However, pancreatic involvement in patients with COVID-19 is rarely reported. Pancreatic symptomology usually corresponds to asymptomatic abnormal pancreatic enzyme elevation and acute pancreatitis. Here, present a rare case of acute pancreatitis in a patient with COVID-19 (Kataria *et al.*, 2020)**.**Despite learning more about this virus every day, the impact of COVID-19 on the pancreas remains less explored.report a patient with COVID-19 who presented with pancreatitis in the absence of respiratory symptoms (Lakshmanan and Malik, 2020)

II. PATIENTS AND METHODS

A . Design of Study

The current study was conducted in Thi-Qar province, A total of 150 sample, 100 sample of patients aged between 37-69 years, including 46 males and 54 females, are in the isolation center for people infected with Corona virus at Al Hussein Teaching Hospital in Thi-Qar and Shatrah General Hospital. The study also included 50 sample control 28 males and 22 females .The period from January2022 to March 2022.

B. Methods

A total of 150 sample, 100 sample of patients aged between 37-69 years, including 46 males and 54 females, are in the isolation center for people infected with Corona virus at Al Hussein Teaching Hospital in Thi-Qar and Shatrah General Hospital. The study also included 50 sample control 28 males and 22 females . after signing consent from the study take . 5 ml of venous blood was collected from patients and control which was added to gel tubes and EDTA tubes ,take 2 ml of blood with EDTA was used to make HBA1c, and another 3 ml of blood was put into a gel tube and then the tube centrifuged at 4000 rpm for 10 min to extract serum for glucose estimation test, and complications were carried out in an apendrof tube for the purpose of error avoidance and compensation if an error occurred and stored at -20°C until used for quantification of immunological parameters (glucagon, PRSS1 protease, serine, 1), all patient and observational data including age, gender, clinical presentation features, patient history, height, and weight were recorded.

C. Statistical Aanalysis

The data of the current study were analysis by using SPSS version 26, based in using independent sample t test, one way ANOVA at P <0.05.

III. RESULT

3.1. Estimation Diabetic Parameters

The current study recorded a significant increase in the percentage of RBS and Hba1c in the sick group, which is diabetic patients with Covid-19, compared to the control group, which is diabetic patients only. It also showed a significant difference in the percentage of random blood sugar and Hba1c at p < 0.05, (as in table 1).

Table (1): RBS and HbA1c Concentration of Covid-19 and DM patients

Diabetic Parameters	Mean ± SD		
	Diabetic with Covid-19 (No.100)	Diabetic patient only (No.50)	p. value
RBS	381.7 ± 65.5	282.9 ± 60.4	< 0.001
HbA1c	9.47 ± 0.99	6.96 ± 0.70	< 0.001

3.2. Pancreatic Hormone

The current result recorded a significant increase in the level of trypsin and glucagon hormone in Covid-19 infected DM, and also showed a significant difference in the percent of Trypsin and Glucagon hormone at p <0.05, (as in table 2).

Table (2): Level of trypsin and glucagon hormone in covid-19 and DM patients.

Pancreatic Hormone	Mean ± SD		
	Diabetic with Covid-19 (No.100)	Diabetic patient only (No.50)	p. value
Trypsin	39.0 ± 12.2	15.9 ± 4.96	< 0.001
Glucagon	64.5 ± 21.6	17.6 ± 4.98	< 0.001

3.3. Estimate Diabetic Parameters According to sex

The current study recorded a significant increase in the rate of blood sugar and HbA1c in males and females of diabetic patients with Covid-19 than in diabetics only who did not have Covid, which is the control group, and it also showed a significant difference in random blood sugar and Hba1c with a value of p < 0.05, (as in table 3).

Table (3) RBS and HbA1c Concentration of Covid-19 and DM patients only according to sex

Diabetic Parameters	Male		p. value	Female		p. value
	Patients	Control		Patients	Control	
RBS	386.3 ± 62.0	284.7 ± 62.0	< 0.001	377.8 ± 68.6	280.3 ± 68.6	0.001
HbA1c	9.60 ± 1.07	6.98 ± 0.71	< 0.001	9.37 ± 0.92	6.92 ± 0.69	0.013

3.4. Pancreatic Hormone according to sex

In the male, the current result recorded a significant increase in the percent of trypsin and glucagon hormone in Covid-19 infected DM, also showed a significant difference in the percent of Trypsin and glucagon hormone at p 0.05. In the female, the current result recorded a significant increase in the percent of trypsin and glucagon hormone in Covid-19 infected DM, also showed a significant difference in percent of Trypsin and glucagon hormone at p <0.05, (as in table 4).

Table (4): Pancreatic hormone in male and female of Covid-19 infected patients compared with DM only according to sex

Hormone Parameter	**Male**	**p. value**	**Female**	**p. value**		
	Patients	**Control**		**Patients**	**Control**	
Trypsin	40.2 ± 11.3	15.5 ± 5.03	< 0.001	38.0 ± 11.9	16.6 ± 4.92	< 0.001
Glucagon	**58.0 ± 16.1**	**17.2 ± 4.18**	**< 0.001**	70.0 ± 21.1	**18.1 ± 5.98**	**< 0.001**

3.5. Estimate Random Blood Sugar According to BMI groups

According to BMI, the results showed a significant increase in the second group of BMI patient, while a non-significant was recorded in control group. The result also noted a significant difference in all BMI groups categories in patients compared with the match in control groups at p <0.05, (as in table 5).

Table (5): Random blood sugar level in Covid-19 infected DM and DM patients only according to BMI

RBS BMI	**Patients**	**Control**	**p. value**
	Mean ± SD		
Under weight	350.5 ± 26.0	270.1 ± 52.8	< 0.001
Normal weight	397.3 ± 50.0	285.7 ± 68.8	< 0.001
Over weight	372.4 ± 86.9	287.2 ± 58.2	< 0.001
p. value	**0.032**	**0.736**	
LSD	**38.3 : NS : NS**	**Non-Sig**	

3.6. Estimate HBA1c According to BMI groups

According to BMI, the results showed a significant decrease in the first group of BMI patient, while a non-significant was recorded in control group.

The result also noted a significant difference in all age groups and BMI categories in patients compared with the match in control groups at p <0.05 as in table (6).

Table (6): HbA1c level in Covid-19 infected D M and D M patients only according to BMI

HbA1c BMI	**Patients**	**Control**	**p. value**
	Mean ± SD		
Under weight	8.82 ± 0.56	6.60 ± 0.61	<0.001
Normal weight	9.63 ± 0.88	7.15 ± 0.78	<0.001
Over weight	9.51 ± 1.17	6.95 ± 0.65	<0.001
p. value	**0.026**	**0.758**	
LSD	**0.58 : 0.60 : NS**	**Non-Sig**	

3.7. Trypsin Concentration According to BMI groups

According to BMI, the results showed a non-significant in BMI group of patient, and a non-significant recorded in control group. The result also noted a significant difference in BMI groups categories in patients compared with match in control groups at p <0.05 as in table (7).

Table (7): Trypsin concentration in Covid-19 infected D M and D M patients only According to BMI groups

Trypsin BMI	**Patients**	**Control**	**p. value**
	Mean ± SD		
Under weight	42.7 ± 10.7	15.3 ± 4.94	< 0.001
Normal weight	37.0 ± 12.9	17.2 ± 5.69	< 0.001
Over weight	40.3 ± 11.5	15.3 ± 4.39	< 0.001
p. value	**0.212**	**0.446**	
LSD	**Non-Sig**	**Non-Sig**	

3.8. Glucagon Concentration According to BMI groups

According to BMI, the results noted a non-significant difference in both patients and control. The result also noted a significant difference in BMI groups categories in patients compared with match in control groups at p <0.05 as in table (8).

Table (8): Glucagon concentration in Covid-19 infected D M(patients) and D M patients only(Control) According to BMI groups

Glucagon BMI	**Patients**	**control**	**p. value**
	Mean ± SD		
Under weight	75.3 ± 14.2	16.9 ± 5.41	< 0.001
Normal weight	65.2 ± 20.6	16.5 ± 4.55	< 0.001
Over weight	59.3 ± 18.9	18.7 ± 5.07	< 0.001
p. value	**0.059**	**0.342**	
LSD	**Non-Sig**	**Non-Sig**	

IV. DISCUSSION

The current study indicated a significant increase in concentration of RBS and HbA1c in Covid-19 infected diabetic patients than diabetic patient only. According to age a non-significant difference was noted in RBS and HbA1c, but according to BMI noted a significant increase in level of RBS and HbA1c in both overweight and obesity group than normal weight.

The current study agreed with study of Kumar and et al, (2021), their study involved inflammatory marker in diabetic and non-diabetic COVID-19, and concluded a Covid-19 infection induce a high level of RBS and HbA1c in diabetic patients compared with patients without Covid-19 infection. Hyperglycemia promotes SARS-CoV-2 replication in human monocytes, resulting in increased viral proliferation Thus, hyperglycemia is an independent risk factor for frequent (Codo *et al* , 2020). Also the current study agreed recent study performed by Smith *et al*,(2021), they study impaired glucose metabolism in patients with diabetes with severe COVID-19, their study investigated a significant increase of diabetic parameters in covid-19 infected patients than diabetic only, also found a positive correlation between BMI and diabetic parameters. A possible explanation for a link between hyperglycemia and ACE2 levels in the severity of COVID-19 disease could be explained by several clinical observations in SARS and preclinical observations in the non-diabetic. Potential changes in glycosylation of the ACE2, as well as glycosylation of the viral spike protein, both possibly induced by uncontrolled hyperglycemia, may alter both the binding of the viral spike protein to ACE2 and the degree of the immune response to the virus*(Smith et al*, 2021) . Several studies showed that DM associated as a distinctive comorbidity increased the morbidity and mortality of COVID-19 patients (Malik and et al, 2022). The current study agreed with the study (Al-Haris and Saleh, 2022) whose study included the pathological bases of severe Corona virus disease -19 in patients with diabetes. This agreement between the two studies is in terms of the rise in the level of Random blood

sugar and Hba1c in patients with Covid, but there is a difference between the high levels In sugar where the current study recorded the level of (RBS 381),(HBA1C 9.47),While their studies recorded less than these levels and as follows(RBS 183),(HBA1C 6.44).

The current study disagreed with previous studies were reported the glucose levels was higher than reported in the current study, the study of Reddy *et al* , (2020), their study recorded the concentration of glucose was 555 mg/dl, while agreed with respect of HbA1c concentration was 14.2 mg/dl. Also, study of Chee and et al, (2020), recorded the glucose level was 714, and HbA1c was 14.2, and study of Kim *et al*, (2020), reported the hyperglycemia in Covid-19 patients was 655 mg/dl and HbA1c was 11.4. in contras the study of Li *et al*, (2020), reported the level of glucose lowest than reported in the present study was noted 298 mg/dl and HbA1c was 6.8.

Diabetes is linked to the severity of infection by a number of factors. Hyperglycemia can initiate, intensify, or extend the acute inflammatory response. It also causes a fibrinolysis and coagulation mismatch, leading to increased factors of coagulation and relative inhibition of the system of fibrinolysis, promoting a state of pro-coagulation.30 Furthermore, SARS- CoV-2 is thought to use ACE2 as an entrance receptor on the islets of Langerhans. This can cause these cells to dawn in a moderate to the severe manner, resulting in mild hyperglycemia and life-threatening diabetic.

The current study showed, according to sex, that the Hba1c level and Random blood sugar increased in diabetic patients infected with the covid19 compared to diabetic patients only, and there was a significant difference between the two groups. Several observational studies have provided clinical evidence that uncontrolled hyperglycemia may lead to a longer LOS and significantly higher mortality in COVID-19 patients. The current study agreed with study of (Yang, Cai and Zhang, 2021). Their study included that high blood sugar in the body leads to a doubling of the symptoms of Covid and leads to death due to the relationship between Covid and high sugar in the body. As for age and body mass, a significant increase was observed in the level of normal sugar and cumulative sugar for diabetic patients with Covid and diabetic patients only. The current study agreed with study of (Abdelaleem *et al*, 2022). Their study included to study Covid-19 related diabetes and try to find predictors of mortality in these patients.

Hyperglycemia is commonly seen in critically unwell patients and can be correlated to disease severity (Chandrashekhar and Pozzilli, 2022).

Our data showed that higher HbA1c levels were a factor in disease severity in patients with COVID-19 and diabetes. These results are consistent with those of previous studies. A retrospective cohort study of the association between pre-infection glycemic control and disease severity in patients with type 2 diabetes and COVID-19 in Israel found a gradual dose–response relationship between HbA1c level and the risk of severe COVID-19*(*Hayek *et al*, 2021). A population-based cohort study in England also suggested a higher risk of mortality from COVID-19 in patients with either type 1 or type 2 diabetes with HbA1c levels >10.0% than in those with HbA1c levels of less than 6.5%(Holman and et al, 2020). In addition, a Japanese study showed that HbA1c levels might be a risk factor for severe disease requiring oxygenation in patients with COVID-19(Yoroidaka, Kurita and Kita, 2022)

The current study indicated a significant increase in concentration of Trypsin and Glucagon hormone in Covid-19 infected diabetic patients than diabetic patient only. According to age a non-significant difference was noted in Trypsin and Glucagon, but according to BMI noted a significant increase in level of Trypsin and Glucagon in both overweight and obesity group than normal weight. The study also showed in the table according to age a significant increase in the level of trypsin and glucagon for the affected group compared to the control group and also according to the distribution of males and females and he same increase occurred.

v. Conclusion

The current study concluded that patients with Covid-19 diabetes have a high level of trypsin and glucagon, and patients with Covid-19 diabetes have a high concentration of glucose and HbA1c, and it was found that body mass and age did not affect the concentration factors.

VI. Acknowledgment

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VII. ETHICAL CONSIDERATION

The ethical permission was obtained from the Al Hussein Teaching Hospital in Thi-Qar and Shatrah General Hospital and from all participants in this work (patients and healthy) to conduct the research.

VIII. Conflict of interest

The authors declare no conflicts of interest

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