



Original Article

Study of Diabetic Imbalance during Acute Phase and Recovery in Patients with COVID-19 in Baghdad/Iraq

Ali Muhsin Hasan^{1,*}, Ahmed Saadi Hassan², Amal Hasan Atiyah³

¹National Center of Teaching Laboratories, Medical City, Baghdad, Iraq

²PhD Chemistry, Health & Medical Technology College, Middle Technical University, Baghdad, Iraq

³Institute of Medical Technology, Baghdad, Middle Technical University, Baghdad, Iraq

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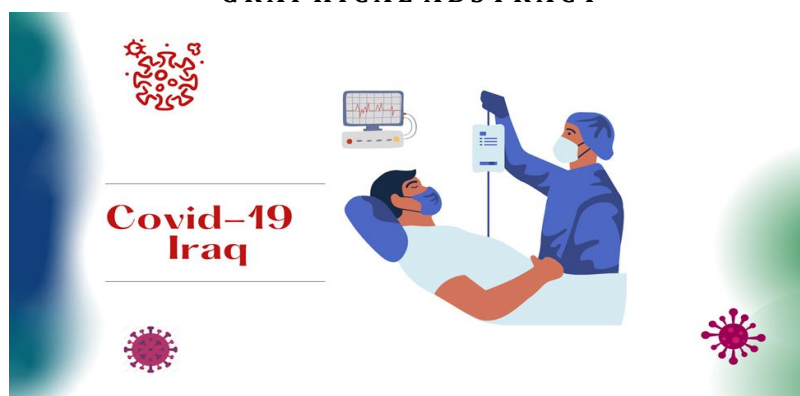
Fructosamine

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ABSTRACT

This study aims to investigate traces of COVID-19 on diabetic profile during infection and after recovery to manifest the effects of disease upon pancreas due to uncensored elevation of glucose level, taking HbA1c, and fructosamine up scores with them, in Baghdad City from October 2021 till April 2022. They were consisted of equal halves of males and females, for both patients and controls. Patients were consisted of 120 individuals with acute to convalescent phase of COVID-19 and 60 healthy controls, all aged between 19 and 61 years. Tests that were depended in this study are: Random blood sugar, RBS, fructosamine, and glycated haemoglobin, HbA1c. Samples are of serum and whole blood for HbA1c that was done by using Roche – Integra 400 plus and G8-TOSOH auto analyzers at Al-Karkh Medical Laboratory in Baghdad.

GRAPHICAL ABSTRACT



* Corresponding author: Ali Muhsin Hasan

✉ E-mail: Email: albayatiali1975@gmail.com

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Introduction

Pancreatic Profile: Pancreas is that exocrine gland lies near stomach and helps to digest food via fluid that pours in duodenum consisted of lipase, protease, and carbohydrase, in addition to the major hormones of insulin and glucagon; as an endocrine gland which are the regulators of body sugar by releasing into cardiovascular system by endocrinal route [1]. Hyperglycaemia or starting diabetes mellitus was the most important risk criteria that COVID-19 left behind after recovery; in addition to being considered as patient with DM, side to side for the secondary infections made a real threaten to life to those who were already at a step of getting more diseases due to their hereditary or environmentally risk factors, like genetic factors or type and site of habitat, making consequences of this disease the worst among other problems that can take effect on renal system; rather than pancreatic cancer [2]. When pancreas get infected or inflamed, by anyhow, it could be chronic, for the least, and acute, for the most cases, in which signs mostly with nausea, vomiting, and epigastric pain, in addition to fever, hypoactive crumps, even jaundice may accompany if it expanded from an obstruction by gallstone. The internal tissue is consisted of sectors with different secretions and functions, called Pancreatic Islets [3]. These islets secrete hormones, like Glucagon from α - Langerhans and Insulin of β - Langerhans; the two main regulators for glucose systemic levels; hence, when infection takes place, or any type of tissue destruction occurs; secretions are going to be impaired or malfunctioned due to cells injury, biologically or chemically, like in case of tumors or as when infection with COVID-19, where extensions of disease might spread to cause acute hyperglycaemia, which strike body and may lead to getting diabetes mellitus after recovery and may permit getting involved with more health misfortune in future [4]. Blood sugar the phrase Glycaemia describes the glucose level in blood stream, where its prescribed by two prefixes; hyper which gives a notice for the elevation of glucose level in blood stream; and hypo as a prefix used for low glucose level in plasma, all the

hormones above, except cortisol are secreted by pancreatic islets; especially α -cells and β -cells where insulin is of the latter one [5]. Any irregularity of glucose level; up or down abnormally; is called Dysglycaemia that mainly consists an impaired morning fasting level, hyperglycemia, bad tolerance test of glucose, and hypoglycemia [6]. Mechanisms to restore glucose levels satisfaction should be very quick and active to maintain the ordinary and normal measurements; whether it was hyperglycemia or hypoglycemia to prevent loss of conscious or seizures, for some factors give a great chance to make disturbances or getting risk to have diabetes mellitus, like obesity or overweight, hypertension, hyperlipidemia, and familiar history of the disease, rather than disorder of thyroid gland, where hyperthyroidism leads to chronic hyperglycemia due to a quick elimination of insulin by elevating metabolism, and vice versa [7]. Hemoglobin glycation occurs mainly to most monosaccharides like fructose and galactose; and firstly of course is glucose; are automatically, non - enzymatically and rapidly bind to hemoglobin; as long as they existed in blood stream. However, glucose binding is less than fructose by (13%) and for galactose with (21%). Thus, this made it clear the cause of considering glucose is the main source of energy rather than these two latter as a monosaccharide [8]. Glycation is the phrase used to describe the attachment of sugars to hemoglobin, for this HbA1c, as mostly called, is in fact a measure of component of hemoglobin of Beta- N-1-deoxy-fructosyl part to investigate the presence of excessive sugar particles in plasma [9]. This phrase, glycation, usually takes place due to reduce the excessive levels of diabetic molecules that may make several complications, totally or partially, for some organs in DM; by consequences or direct act. Since it occurs with protein or lipid in blood stream and makes damage or even to thin collagen of vascular system causing elevated and uncontrolled blood hypertension due to the high presence of glucose or fructose which can attach about ten times higher than glucose, because the latter is energy source stored for emergency [10]. There is a limitation for this test which is linked due to life

span of red blood corpuscles of 4 months. Hence; it is done to perform three-months measurement control and monitoring for diabetic people as a Glycemic control, as long as its level is normal for ordinary individuals, but if it increases due to the presence of glycated fragments in blood stream, it would give an indication about poor control for diabetes mellitus patients, because the fragments are in a predictable criteria, in addition to association with nephropathy, cardiovascular disturbances, neuropathy, and retinopathy [11]. In another way, glycated Hb may cause damage by atherosclerotic formation of plaque by inflammation, while by another route, molecules of Hb are clumping to each other and to release Quadric-ferric-Hb; Fe^{+4} -Hb, into the sub-endothelium of veins and arteries to increase its permeability to defending cells, and by this way, the loss of ferric ions will continue by excitation of Fe^{+2} through Fe^{+3} to the abnormal Ferryl-Hb; Fe^{+4} -Hb [12]. Proteins glycation occurs frequently, and it is non-enzymatically if it was with Hb by condensation reaction between N-terminal of β -chain and glucose; by further reactions; it gives glucose molecules to attach to red blood corpuscles when it is in a high level [13]. Whenever plasma glucose levels are with high ranges, and hyperglycemia takes place more often, the more glycation occurs and gives higher readings during testing of HbA1c. Thus, due to increased level of glucose during COVID-19; HbA1c became undependable as monitoring score for DM patients or as an alarm test for pre-diabetic people [14]. The fructosamine molecules are formed via glucose inside blood stream, by its group of carbonyl that reacts and binds to residues of protein amino debris which leads to form Schiff's base, and they are also a kind of Macromolecules-Alkone-Amines-Compounds, MAAC, which have about 1-3 weeks of life span [15]. By anyhow, fructosamine is combined to complications with microvascular dysfunctioning; both in suffering diabetes and non-diabetic individuals; where the more fructosamine was higher; the more cardiovascular problems; disease, congestion, stroke, or even death [16]. People with elevated concentration of fructosamine were more in risk

in years forward to get type II of diabetes mellitus, if that was descended from their grandparents along [17]. While women were at a higher risk in getting mortality chances by cardiovascular causes more than men, for those with a high level of fructosamine and weight [18]. Importance of glycation process occurs to excess of diabetic subjects. It has an adverse effect on several major organs and is at least partially responsible towards some of the major long-term complications in diabetes. Many of its effects are mediated by its consequences on the microvasculature [19].

Materials and Method

Patients were consisted of 120 patients with acute to convalescent phase of COVID-19 and 60 healthy controls, all were in the age range of 19 to 61 years old.

They were consisted of equal halves of males and females, for both patients and controls to keep in touch for getting tests during acute and recovery phases, and to prevent loss of patients; as could as possible; for a period lasted for about 1-3 weeks in acute phase and 4-6 weeks in recovery phase.

Study design was based upon the manifestation of tests that can give an indication for an important signal towards decision about the lineage of infection with COVID-19, the degree of incidence, and intensity. This is a novel study in Iraq via this linkage and comparison.

Samples were drawn and tested directly after getting serum from venous blood in a 6 mL gel tube for RBS and fructosamine by using biochemistry auto analyzer Roche-Integra 400 plus and 3 mL whole blood for HbA1c by using G8-TOSOH auto analyzer.

Results and Discussion

Study of patients

Victims of COVID-19 were of different age groups and both genders. Therefore, by calculating the collected data, the findings can be as follow: patients were 120 people divided into two halves of males and females; with 60 healthy individuals taken as controls taken after excluding their resent and the previous infection with COVID-19

by maintaining antibodies against it of both (IgM) and (IgG), respectively.

The age of study samples was normally distributed and ranged from (19-61) years old, with a mean of (35.67 ± 9.137), and most of the sample at the age group of (20-29) years old with (36.7%) for females, while it was of (40->50) years old with (45%) for males.

The mean age of cases group was (36.92 ± 9.242) years old mostly at the age group of (30-39) and (>40-50) years old (26.7%) which were equal in

mean of infections due to be the highest group in the working field.

While that of controls was (33.17 ± 8.452) years old mostly at the age group of (20-29) years; (43.3%) for females, while males are of (30-39) years; (36.7%); with significant mean differences among them of 3.758; ($t = -2.645$, $df:178$, $P=0.009$). Otherwise, no significant differences were identified regarding the age groups of study samples ($P>0.05$), as presented in [Table 1](#), matching with [20].

Table 1: Distribution of studied groups based on the age groups (year) and gender

Studied groups	Gender		Age groups (Years)			Total
			(<20-29)	(30-39)	(40->50)	
COVID-19 Patients	Female	No.	22	21	17	60
		%	36.7%	35.0%	28.3%	100.0%
	Male	No.	10	23	27	60
		%	16.7%	38.3%	45.0%	100.0%
Control	Female	No.	13	11	6	30
		%	43.3%	36.7%	20.0%	100.0%
	Male	No.	10	11	9	30
		%	33.3%	36.7%	30.0%	100.0%

For pancreatic profile tests, the comparison between males and females in acute stage was as follow: Initially, [Table 2](#) represents the statistical calculations for Random Blood Sugar, RBS, glycated haemoglobin, HbA1c, and fructosamine in the first 1-3 weeks of infection which is called The acute phase where it scored a highly significant elevation in levels of these test with those of controls, healthy people who do not have neither COVID-19; nor any chronic diseases. Hence, noticeably males are of higher scores than females, some linked these differences with hormones, body mass, and type of diet, while others put an idea of having monthly menses that re-new body tissues and re-stimulate further organs in this event, defending the creature who bears and raise babies to create a newer generation for humanity [21].

Males are more affected by COVID-19 than females in all tests pancreatic profile with a remarkable difference, except fructosamine which gave the notice to accumulated problems to pancreatic functions, especially by elevating

RBS and HbA1c to the upper limits compared with females [22].

The statistical criteria of the acute phase for significance of test, in addition to means of age and levels, getting highly significant scores of ($P<0.01$), HS for all tests of profile with no consideration to gender ([Table 3](#)).

This statistical table is special and owned for this study with no consideration to other studies or researches.

As listed in [Table 4](#), the data shows an alternation in the levels of blood glucose towards decrement; mostly related to diet and assurance of females to get thinner after gaining some kilos due to stay quarantined or less movement behavior. However, HbA1c and fructosamine still elevated even after recovery, due to the disturbance had occurred for pancreatic tissues caused by increased duties during acute phase of disease and persisted mechanical re-arrangement after recovery, which scored increased cases of tiredness after weeks of staying home or at hospitals.

Table 2: Comparison of the pancreatic levels (RBS, HbA1c, and fructosamine) between males and females for acute phase during 1-3 weeks of COVID-19 patients

Pancreatic	Gender	Mean ±Std.	t-test	P-Value
RBS (mg/dl)	Female	203.95±68.26	8.037	.000*
	Male	379.93±155.27		
HbA1c (%)	Female	5.73±0.56	5.645	.000*
	Male	6.5633±0.99		
Fructosamine (µmol/L)	Both	288.80±57.14	5.375	.000*

*This sign means that p-value is highly significant (HS)

Table 3: Comparison of the pancreatic levels (RBS, HbA1c, and fructosamine) and age (year) for acute phase during 1-3 weeks of COVID-19 patients

	Age (year)	RBS (mg/dl)	HbA1c (%)	Fructosamine (µmol/L)
Mean ±Std.	36.93±9.24	291.95±148.56	6.15±0.91	230.90±20.00
t-test		19.105	36.945	33.165
P-Value		.000*	.000*	.000*

*This sign means that p-value is highly significant (HS)

Table 4: Comparison of the levels of pancreatic (RBS, HbA1c, and fructosamine) between males and females for recovery phase after 4-6 weeks of COVID-19 patients

Pancreatic	Gender	Mean ±Std.	T-test	P-Value
RBS (mg/dl)	Female	111.52±3.85	7.045	.000*
	Male	185.10±9.71		
HbA1c (%)	Female	6.51±0.10	6.159	.000*
	Male	7.96±0.21		
Fructosamine (µmol/L)	Both	352.02±100.15	6.542	.000*

*This sign means that p-value is highly significant (HS)

Therefore, males were near or above the normal ranges which made them at higher risks for future diabetic expected problems [23]. Table 5 indicates a high significant relationship

alternation in level of serum fructosamine with highly significant relationship stayed for RBS and HbA1c, as concerned with this study.

Table 5: Comparison of the pancreatic levels (RBS, HbA1c, and fructosamine) between males and females for recovery phase after (4-6) weeks of COVID-19 patients

	Age (year)	RBS (mg/dl)	HbA1c (%)	Fructosamine (µmol/L)
Mean±Std.	36.93±9.24	148.31±67.90	7.23±1.48	352.02±100.15
t-test		18.338	35.691	24.050
P-Value		.000*	.000*	.000*

*This sign means that p-value is highly significant (HS)

Conclusion

COVID-19 has very high effects in the process of glycation occurred during the infection for diabetic molecules. Several major organs suffered an adverse effect, or it became a part of it for long-term major consequences for DM and microvasculature. HbA1c is not dependable as

before to judge actuality of having DM after COVID-19; not like fructosamine which was more stable after infection than HbA1c. Reducing fructosamine particles had an effective positive prognosis to prevent such complications on heart muscle and kidneys.

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Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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