The Correlation Study between Some Biochemical Parameters of 256 Covid-19 Cases Considering Diabetes

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Abstract

Background: Diabetic Mellitus is an independent risk factor in patients with coronavirus disease 2019 (COVID-19), but data on the association of diabetes, acute kidney injury, and COVID-19 severityare limited to Middle East populations.

Materials and Methods: This cohort study aimed to investigate these associations in 256 patients sequentially admitted between June 2020 and November 2020, at Emirati Hospital/Erbil. The investigation included some main biochemical parameters including liver and kidney function tests. Data analysis was processed by SPSS and the Pearson correlation pathway using log-converted data.

Results: Diabetic patients showed the highest correlations between measured parameters, of which glucose level showed a positive correlation coefficient (0.13**) with C-reactive protein and other biochemical parameters. Based on the glycemic status, COVID-19 patients were found in 3 groups, euglycemia group with an abundance of 148 (57.81%),hyperglycemiapatients were 67 (26.17%), and 41 of them were diabetics (16.01 %).

The Diabetic group showed a significantly (0.0002) increased level of C-reactive Protein and Glucose in comparison with hyperglycemia [CRP 15.38 mg/dl vs 10.09mg/dl, glucose 429.75 mg/dl vs 160.62mg/dl] with a Significantly (0.00374) higher mortality rate (29.26%) than that (10.44%), and (6.75%) of hyperglycemia, and euglycemia, respectively.

Conclusion: Male COVID-19 cases showed higher correlations between the estimated parameters than female cases. Diabetes was significantly associated with elevation of almost all kidney and liver function parameters. Finally, diabetes followed by COVID-19 disease was related to severe complications and higher mortality rates than nondiabetic COVID-19 cases.

Keywords:*Biochemistry,COVID-19,Diabetes, Kidney and liver injury, correlations*

Introduction

A new viral infection known by the coronavirus (COVID-19) has invaded Wuhan, China, in December 2019 [1]. Zoonotic exposure led to the transmission of coronavirus (COVID-19), resulting in the current pandemic disease.[2] After one year, since the first case announcement, the total COVID-19 cases in December 2020, has reached 75 million reported cases and 1.6 million deaths of Novel COVID-19 disease. [3]

Diabetic disease is considered a chronic disease that results from either complete lack of insulin (type 1 diabetes) or resistance to insulin (type 2 diabetes)[4]. diabetics are more vulnerable to multiple infectious diseases, eventually, damaging to their immune system

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and even causing organ failure, resulting in higher mortality rates as in COVID-19 patients.[4] In addition, the death incidence of 27955 Italian diabetes by COVID-19 was 31.1%. This has risen in another survey in the UK, the prevalence death of 23804 British diabetes by COVID-19 was 32%,[5] while another study showed 22% of death occurrence of diabetes with confirmed COVID-19 cases among 52 intensive care unit patients in China. [6]

Acute kidney injury (AKI) incidence in COVID-19 disease was varied as evidenced by Chinese, invasion of COVID-19 virus into kidney tissue[7,8]. clinical epidemiology of COVID-19–associated acute kidney injury (AKI) across our health system later also has been reported. [9,10] A rapid increased serum urea and creatinine levels caused a hypercatabolic state in which understanding the causes will help as a marker for disease severity, predicting pulmonary or kidney outcomes[11]. Previous study published different incidence rates of AKI from only 0.5% among 1099 patients, 11 to 22.2% in 3908 patients with a 75% mortality rate.[12] A recent cohort study on 3200 patients with COVID-19, showed that closely half of them had AKI and acute dialysis.[13] Therefore, exploring the biochemistry of COVID-19 patients with diabetes will aid the physicians to reduce the incidence of severity. A retrospective study on 256 COVID-19 after confirmation by Real-time polymerase chain reaction (PCR) in one hospital was made and the correlations between estimated biochemical parameters were discussed.

Materials and method

Data collection

A total of 256 Admitted patients between June 2020 and November 2020, at Emirati hospital/Erbil, were enrolled in this study. After confirmation of Real-time polymerase chain reaction positivity for COVID-19 infection, the patients were separated into males (157) and females (99). Based on the glycemic status, COVID-19 cases were divided into 3 groups, euglycemia group (had normal blood sugar level before and during hospitalization), hyperglycemia group (increased blood glucose during hospitalization with no history of diabetes but their blood sugar normalized after hospital discharge), and Diabetes group had Elevated blood glucose level with a history of using diabetic treatments). Blood Samples were taken to the laboratory for examination of high sensitive C-reactive protein (hs-CRP), alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), total bilirubin (TBILL), Direct bilirubin (DBIL), Urea, and Creatinine by the biochemical auto analyzer (Cobas - Roche C 311, Hitachi company, japan). [14]

Statistical Analysis

Data processing was made by SPSS (0).21 (IBM, Armonk, NY, USA). The Undistributed data were converted into a log 10 scale. The relation between the parameters was found by the Pearson correlation pathway using log-converted data. [15]

Results and Discussion

The Data analysis in Table 1. shows that among the 256 included cases of COVID-19, 157 of them were males (63.33%) with an average age of 56.13 years, and 99 of them were female (38.67%) with an average age of 53.62 years. As illustrated in (table 2), from a total of 256 COVID-19patients, 148 of them were euglycemia (57.81%), 67 of them were hyperglycemia (26.17%), and 41 of them were diabetics (16.01 %). the average age was higher in diabetic patients (55.68 years) than those of euglycemia (48.12years)and hyperglycemia (51.08years), respectively. Males have outnumbered females with no significant differences on the estimated parameters. Diabetes was associated with significantly higher mortality rates (29.26%) than that of hyperglycemia (10.44%), and euglycemia(6.75%), respectively (Table 2), (Figure 1). The displaced laboratory results in (Table 1) show that the levels of Urea, creatinine, AST, ALT, TBILL, DBILL, ALP, and CRP were higher nonsignificantly in male COVID-19cases than that of female cases.

Table 1. Statistical findings of the Age and biochemical parameters based on gender.

parameter	Gender	N	Mean	SEM	STDev	Min	Max	p (Log10)
Age (Year)	Male Female	157 99	56.13 53.62	0.42 0.73	5.27 7.27	39 45	65 68	0.175679
Urea(mg/dl)	Male Female	157 99	47.62 44.83	2.61 3.42	32.71 34.03	14 8.7	285.9 280.2	0.965922
Creatinine(mg/dl)	Male Female	157 99	0.61 0.6	0.03 0.04	0.42 0.44	0.4 0.2	4.83 3.13	0.376927
AST(mg/dl)	Male Female	157 99	43.54 38.6	2.66 2.97	33.33 29.55	13.6 13	287.1 159.9	0.409090
ALT(mg/dl)	Male Female	157 99	50.98 36.03	3.62 3.56	45.33 35.41	20 18	283.5 300.7	0.209749
TBILL(mg/dl)	Male Female	157 99	1.35 1.05	0.09 0.10	1.19 1.01	0.3 0.2	12.2 8.4	0.911234
DBIL(mg/dl)	Male Female	157 99	0.38 0.36	0.02 0.02	0.23 0.18	0.24 0.18	1.45 1.37	0.819219
ALP(mg/dl)	Male Female	157 99	105.8 96.97	5.46 5.02	68.42 49.97	76.1 44	705.2 394.9	0.187637
CRP(mg/dl)	Male Female	157 99	10.53 8..95	0.39 0.49	7.60 6.83	1.1 0.9	25.8 21.2	0.125642

Note: Mean ± standard deviation in COVID-19–positive patients.

Data analysis in Table 2. showed significantly (p-value =0.002) higher urea values in diabetes 58.75 (27.3-132.4)mg/dl than that of 49.03(23-151) mg/dl, 37.09(17-104)mg/dl, for Hyperglycemia and euglycemia, respectively. Creatinine was significantly (p-value=0.00236) higher in the diabetic group 0.807 (0.5-3.3)mg/dl than that of 0.60 (0.3-2.9)mg/dl, 0.57 (0.3-2.7)mg/dl for Hyperglycemia, and euglycemia, respectively. The Diabetic group showed significant (0.0002 and 0.001) differences in the level of CRP and Glucose, respectively, in comparison with hyperglycemia [CRP 15.38 (3.1-25.8) vs 10.09 (1.8-17.1), glucose 429.75(276-580) vs 160.62(120-213)] mg/dl and euglycemia group [CRP 15.38 (3.1-25.8) vs 8.33 (1.6-16.3), glucose 429.75(276-580) vs 91.49 (54-115)]mg/dl. Insignificant changes existed in other tested parameters, such as AST, ALT, TBILL, DBIL, and ALP levels.

Table 2. Laboratory findings of three COVID-19groups based on the glycemic status.

Parameter		Euglycemai (n= 148)	Hyperglycemia(n= 67)	Diabetics(n= 41)	P-value
Age		48.12(37-56)	51.08 (44-63)	55.68 (47-68)	0.26545
Gender	Male (n,%)	82 (55.40%)	38 (56.71%)	23 (56.09%)	0.18743
	Female (n, %)	66 (44.59%)	29 (43.28%)	18 (43.90%)	0.17659
Mortality rate (n, %)		10 (6.75%)	7 (10.44%)	12 (29.26%)	0.00374
Urea (mg/dl)		37.09 (8-104)	49.03(23-125)	58.75 (27.3-132.4)	0.00061
Creatinine,(mg/dl)		0.57 (0.3-2.7)	0.60 (0.3-2.9)	0.807 (0.5-3.3)	0.00236
AST,(mg/dl)		38.91 (17.9-154)	45.23(23-137.7)	39.91(17.8-94.7)	0.39567
ALT (mg/dl)		40.33(20.9-184)	42.94(26-300)	41.11(21-128.6)	0.35239
TBILL (mg/dl)		0.98(0.3-8.4)	1.21(0.3-2.1)	1.114(0.4-3.4)	0.82398
DBIL (mg/dl)		0.33 (0.12-0.79)	0.45(0.24-1.22)	0.301 (0.13-0.45)	0.79437
ALP (mg/dl)		112.5 (59.7-163)	104.95(38-223)	106.31(80-394.9)	0.20547
CRP (mg/dl)		8.33 (1.6-16.3)	10.09 (1.8-17.1)	15.38 (3.1-25.8)	0.0002
Glucose (mg/dl)		91.49 (54-115)	160.62(120-213)	429.75(276-580)	0.0001

Data are shown as medians and interquartile ranges.

In male COVID-19patients, the analyzed data anticipated the positive correlation coefficient (r-value) between urea (0.69), AST (0.37), DBIL (0.22), and CRP (0.039). While DBIL had a positive correlation with Urea (0.22), creatinine (0.21), and TBILL (0.28), and negatively correlated with the AST (-0.02) and ALP (-0.03). CRP values showed significant relations with the Urea (0.39) and creatinine (0.40) numbers, Table 3. The measured parameters showed fewer correlations in the female cases, which only AST had a significant correlation coefficient (r-value) with the Urea (0.21) and creatinine (0.21) numbers. And, ALT was significantly correlated with ALP (0.22) and AST (0.64) as shown in table 4.

Table 3. Correlation findings detected in the male patients.

Parameter (mg/dl)	Urea	Creatinine	AST	ALT	TBILL	DBIL	ALP
Creatinine	0.69** **0.001** 157						
AST	0.37** **0.001** 157	0.24** **0.001** 157					
ALT	0.13 0.09 157	0.06 0.44 157	0.60** 0.001 157				
TBILL	0.04 0.59 157	-0.15 0.07 157	0.14 0.09 157	0.03 0.71 157			
DBIL	0.22* **0.01** 157	0.21* **0.01** 157	-0.02 0.79 157	0.08 0.33 157	0.28** **0.001** 157		
ALP	0.08 0.33 157	0.11 0.18 157	0.16 0.05 157	0.14 0.08 157	-0.07 0.42 157	-0.03 0.42 157	
CRP	0.39** **0.001** 157	0.40** **0.001** 157	0.15 0.06 157	0.06 0.49 157	0.08 0.32 157	0.08 0.34 157	0.04 0.63 157

*< 0.05; **< 0.01. The Bold values represent statistically significant findings. The first line shows the r values, the second line for p values, and the third line is for patient numbers in all correlations included.

Table 4.Correlation findings detected in the female patients.

Parameter(mg/dl)	Urea	Creatinine	Got	GPT	TBILL	DBIL	ALP
Creatinine	0.81** 0.001 99						
AST	0.21* 0.04 99	0.21* 0.03 99					
ALT	0.07 0.46 99	0.07 0.51 99	0.64** 0.001 99				
TBILL	-0.01 0.90 99	-0.19 0.06 99	0.11 0.26 99	0.01 0.96			
DBIL	-0.04 0.71 99	0.12 0.24 99	0.11 0.29 99	-0.02 0.84 99	-0.02 0.86 99		
ALP	0.35 0.15 99	0.40 0.12 99	0.30 0.06 99	0.22* 0.03 99	-0.13 0.20 99	0.13 0.19 99	
CRP	0.31 0.34 99	0.37 0.38 99	0.43 0.36 99	0.28 0.21 99	0.06 0.57 99	0.14 0.16 99	0.36 0.23 99

*< 0.05; **< 0.01. The Bold values represent statistically significant findings. the first line shows the r values, the second line for p values, and the third line is for patient numbers in all correlations included.

Diabetic patients showed the highest correlations between measured parameters, of which glucose value had positive correlation coefficient (r value) with urea (0.22**), creatinine (0.17**), AST (0.19**), ALT (0.03*), DBIL (0.02**), ALP (0.05**), and CRP (0.13**) levels. CRP values showed significant correlations with the Urea (0.32**), Creatinine (0.27**), AST (0.31**), and ALT (0.15*) levels. ALP was significantly associated with creatinine and Urea(0.24**), AST (0.23**), and ALT (0.19*). No significant relationship was detected between TBILL and other chemical parameters (except for DBILL). And finally, Creatinine values were found to be negatively correlated with the TBILL values (-016*), Table 5.

Table 5.Correlation findings detected in the Diabetic patients.

Parameter (mg/dl)	Urea	Creatinine	AST	ALT	TBILL	DBIL	ALP	CRP
Creatinine	0.59** **0.0001** 16							
AST	0.30** **0.0003** 16	0.13 0.0686 16						
ALT	0.14 0.0532 16	0.05 0.5607 16	0.59** **0.0001** 16					
TBILL	0.05 0.7234 16	-0.16* **0.0445** 16	0.21* **0.0231** 16	0.04 0.6891 16				
DBIL	0.08 0.1969 16	0.23** **0.0078** 16	0.08 0.3791 16	0.06 0.3953 16	0.16* **0.025** 16			
ALP	0.24* **0.0342** 16	0.24 **0.0071** 16	0.23* **0.0219** 16	0.19* **0.0346** 16	-0.04 0.3458 16	0.05 0.6673 16		
CRP	0.32** **0.0018** 16	0.27** **0.0039** 16	0.31** **0.0008** 16	0.15* **0.0452** 16	0.11 0.1457 16	0.15 0.0967 16	0.17 0.0762 16	
Glucose	0.22** **0.0003** 16	0.17** **0.0001** 16	0.19** **0.0024** 16	0.03** **0.0099** 16	0.02 0.68 16	0.02** **0.0002** 16	0.05** **0.0003** 16	0.13** **0.0022** 16

*< 0.05; **< 0.01. The Bold values represent statistically significant findings. Gender discrimination did not consider, the first line shows the r values, the second line for p values, and the third line is for patient numbers in all correlations included.

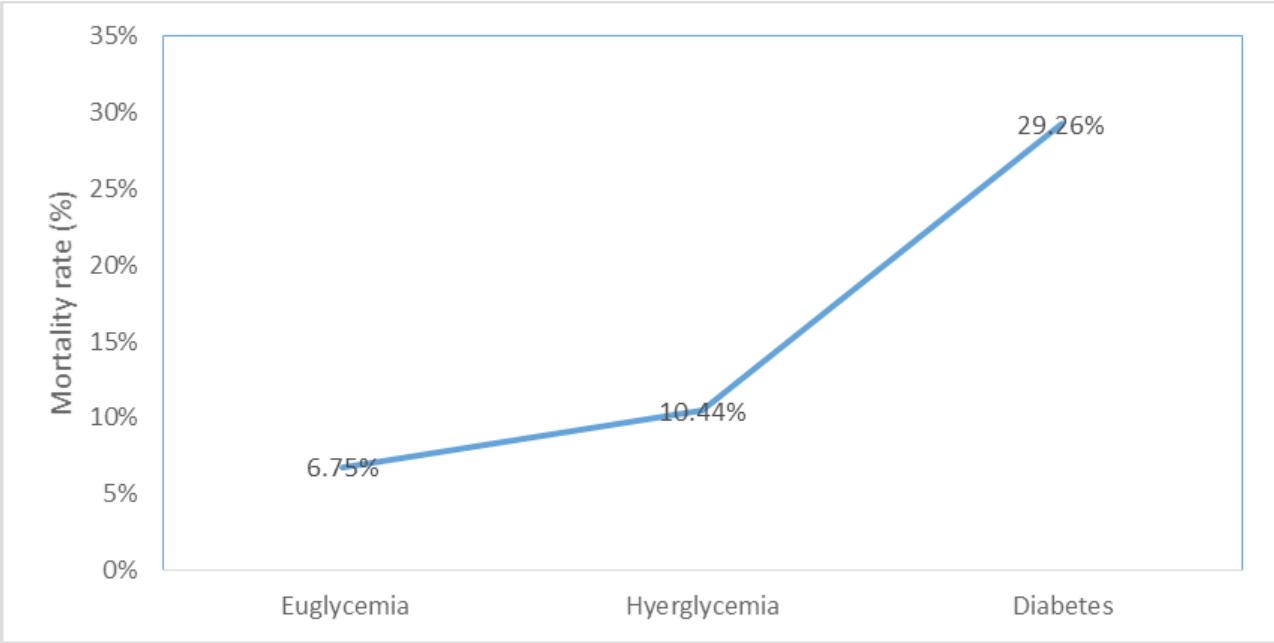

Figure 1. Shows the mortality rate in the COVID-19group according to the glycemic levels.

Coronavirus is a multiorgan inflammatory disease, specialized from another virus of their family, by its rapid spreading, highly contagious, and more vital to the respiratory system with higher mortality rate than previous virus outbreak[16]. Our data showed that the biochemical parameters did not change significantly based on gender. The same was found by other researchers [17].

Men were more common in all three glycemic groups. Our results showed that men COVID-19 patients had higher correlations between their biochemical parameters, specifically urea and creatinine values, which in severe cases may lead to acute kidney injury. By our outcome, previous reports also concluded that regardless of age, men are at higher risk for more severe results with a higher incidence of death than women [18]. Our data showed that diabetes comprised 16.01 % of COVID-19 patients, a percentage that agreed with previous reports regarding the proportion of current pandemic with diabetes [12]. Previous reports of 52 and 99 COVID-19 Chinese cases by Yan et.al [19] and Chen et. al [20], showed the prevalence of 17 and 12.1% of diabetics, respectively. The same was found by previous research work [21].

Based on the glycemic status, the current work showed significant differences in the levels of CRP, glucose, and kidney function parameters (Urea and creatinine) between the three tested groups, in which the values were significantly higher in groups with higher sugar levels (Hyperglycemia and diabetics) in compare with euglycemiaCOVID-19 patients. This may explain the elevated mortality (29.26%) in diabetic group in our data analysis. Such an increased mortality rate in diabetic patients is following a previous study, which proposed a mortality rate of diabetes with COVID-19 disease between 20-32% in different countries according to COVID-19 severity and poverty status [5,22].

Studies showed that increased glycemic status is an independent risk factor of mortality and in the case of COVID-19 patients, causing severe complications because of increased releasing of glucocorticoids and catecholamines into circulation. also led to an increase in the glycation end products and worsened prognosis [23]. Another study showed that increased ACE2 (Angiotensin-converting enzyme2) receptors in hyperglycemia and diabetic patients facilitateCOVID-19 virus adherence to the pancreatic cells leading to decreased insulin secretion by β-cells and thus raising

the severity of COVID-19 infection in those patients [24,25]. Another reason behind the high mortality rate in diabetes may be due to impaired leukocyte function of phagocytosis leading to increased viral infections. In addition, increased cellular binding affinity, decreased viral clearance, reduced T-cell function, and increased susceptibility to hyper-inflammation, and renin-angiotensin-aldosterone system (RAAS) activation are other causes behind the high mortality rate of diabetes followingCOVID-19 disease [25]. The abundance of Dipeptidyl Peptidase-4 which degrades incretin[25] and furin[26] in diabetic patients, is another entry enhancement for coronavirus. Diabetes also has different lung volumes and pulmonary diffusing capacity that also affects their severity level of COVID-19 disease [27].

Our data analysis showed that the level of urea and creatinine positively correlated with the CRP and almost all other estimated parameters without gender discrimination. Diabetes had significantly higher levels of urea and creatinine than those of the euglycemia and hyperglycemia groups. The same result was found by the previous researchers [28]. Previous studies also showed kidney dysfunction and acute kidney injury (AKI) occurrence in a range of 3-9% with 3-fold higher odds of death than COVID-19 without AKI [29]. Studies on hospitalized patients with COVID-19 disease reported that 44%,[30] and 63% [31], of them had proteinuria and significantly increased serum creatinine and blood urea nitrogen levels. Thus, AKI is considered as an independent risk factor of death with or without COVID-19 [30]. A recent study considered the kidney as a target organ of the COVID-19 virus after successful isolation of the virus in the urine sample of an infected patient [32]. Pathogenesis between the current virus and AKI may be also due to sepsis occurrence heading to cytokine storm syndrome [33].

Conclusion

The COVID-19 pandemic still has many unraveled sites that need to be undertaken. As shown from our results that the gender has no significant effect on the severity and progression of COVID-19 disease, although more correlations between biochemical parameters were found in males than in females. The presence of Diabetic Mellitus followed by COVID-19 disease will increase the odds to possess severe complications of liver and kidney organs. C-reactive protein and glucose levels of diabetic COVID-19 patients were positively correlated with almost all estimated biochemical tests, which could be the reason behind the higher mortality rates of diabetes than those of euglycemia and Hyperglycemia COVID-19 patients. The severity of COVID-19 and increased levels of CRP was associated with increased levels of urea and creatinine regardless of gender or glycemic status, which may be referred to an important indications of acute kidney injury. Due to data limitations, some laboratory tests were not included. More elaborate research trials are still required to anticipate other postulates related to correlations between COVID-19, diabetes, and acute kidney injury.

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