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Original Article

Evaluation of Kidney Function Characteristics of 250 COVID-19 Patients with Diabetic Kidney Disease in Hilla Province

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Abstract - The etiology of Coronavirus Disease 2019 (COVID-19) can be attributed to severe acute respiratory disease caused by Coronavirus 2, often known as SARS-CoV-2. The impact of renal function on the prognosis of this condition remains uncertain despite its rapid global dissemination and significant morbidity and mortality. There is an association between decreased renal function and increased death rates in the whole population and a prognostic significance in the context of COVID-19. The prevalence of impaired renal function is frequently observed among the aged population, prompting our investigation into the possible implications of this condition on mortality rates. This study aimed to determine the risk factors and variables associated with COVID-19 in hospitals among patients with diabetes and Chronic Kidney Disease (CKD). Study: During the period from February to April 2022, 250 people diagnosed with COVID-19 were admitted to Hilla Hospitals for Internal Medicine, located in Hilla province. The research encompassed a sample size of 250 people diagnosed with COVID-19, consisting of 130 males and 120 females. The age range of the participants ranged from 20 to 80 years. The mild-to-moderate category accounted for 170 cases, 68% of the total, while the severe category accounted for 80 cases, or 32%. The findings of the present investigation indicate significant alterations in blood parameters, including urea, creatinine, D-dimer, and blood glucose, in different stages of COVID-19 infection, namely mild, moderate and severe.

Keywords - COVID-19, Kidney, Diabetes, Urea, Creatinine.

1. Introduction

China has recorded many New Coronavirus Pneumonia (NCP) cases since December 2019 [1]. Subsequently, the Coronavirus Disease 2019 (COVID-19) rapidly spread rapidly worldwide. Individuals infected with the SARS-CoV-2 virus can experience many outcomes, including lung infection, the need for intubation, and possibly life-threatening consequences. According to research conducted by the World Health Organisation, individuals who are 65 years of age or older, along with those who have preexisting clinical conditions such as Diabetes Mellitus (DM), Chronic Kidney Disease (CKD), and heart disease, demonstrate increased susceptibility to severe manifestations when exposed to the COVID-19 virus. Leon-Abarca et al. [2] also presented findings indicating a significant incidence of morbidity and mortality. Therefore, it is imperative to do a thorough assessment to examine possible correlations between elevated mortality rates among people with diabetes, Diabetic Kidney Disease (DKD), and COVID-19 [3].

The prevailing consensus acknowledges that SARS-CoV-2 predominantly impacts respiratory cells, but it is vital to recognize that it can damage other organs, including the kidneys, ileum, and heart. According to the results

of a recent study conducted by Zou et al. [4], it has been established that the kidneys are more vulnerable to injury, as evidenced by the up-regulation of Angiotensin-Converting Enzyme 2 (ACE2). The existing knowledge on the potential direct implication of the kidneys in COVID-19 needs to be more conclusive. However, Naicker et al. [5] have documented instances where causes such as cytokine storm syndrome have been observed as a consequence of sepsis or direct viral injury to renal tubular cells. Currently, it has been shown that most people affected by COVID-19 exhibit acute renal damage. However, there are situations in which macroalbuminuria, proteinuria, and hematuria may be associated with endothelial dysfunction documented in these individuals [6].

According to a study conducted by Becerra-Munoz et al. [7], previous investigations have indicated that the incidence of Chronic Kidney Disease (CKD) upon hospital admission due to COVID-19 in people 65 years and older was found to be 11.4 %. Furthermore, the development of Acute Kidney Injury (AKI) in this population ranged from 24.8 to 39 %. The association between advanced age and the reduced estimated Glomerular Filtration Rate (eGFR) below 60 has been extensively studied and established as a significant risk factor for mortality in COVID-19. This relationship has been confirmed in various studies, including those conducted by Uribarri et al. [8], Lim et al. [9], and Hirsch et al. [10]. Furthermore, both risk factors are associated with the development of Acute Kidney Injury (AKI) and subsequent mortality. Furthermore, it has been observed that older people diagnosed with COVID-19 tend to exhibit elevated blood creatinine levels upon admission [11]. Examination of the graded correlation between the decrease in estimated Glomerular Filtration Rate (eGFR) and mortality in elderly individuals with COVID-19 has been conducted exclusively by the Collaborative Geriatric Medical Group and Xu et al. [12].

The overall fatality rate of this virus is reported to be 3.4%, with a higher incidence observed among elderly individuals and those with preexisting medical issues, as documented by Ghany et al. [13]. Within this particular setting, the present study conducted a retrospective analysis to assess the biochemical markers of people diagnosed with COVID-19, categorizing them into two groups: survivors and no survivors. This investigation aimed to identify significant factors and facilitate the timely implementation of appropriate therapeutic interventions. Consequently, we evaluated various biochemical indicators through kidney function tests to achieve this goal and gather relevant data, including urea and creatinine levels. However, a limited body of research has examined and compared biochemical markers in patients with COVID-19 with respect to their reference ranges and mortality rates. The relationship between biochemical markers and the death rate in Iraq remains unexplained. Hence, the main objective of this study was to assess serum levels of these indices to improve the care of patients with COVID-19.

2. Methods

2.1. Samples Collection

Two hundred and fifty samples were collected in a general hospital in Babylon, Iraq, from November 20, 2021, to March 30, 2022. The sample consisted of 130 male and 120 female participants, ranging in age from 20 to 80 years. A data set containing biochemical values and demographic data was obtained for 250 individuals through electronic medical records. Due to the retrospective nature of this study, the patients were not exposed to any potential harm, and there was no direct interaction between the patients and the controls. Laboratory-based confirmation of COVID-19 depended on detecting SARS-CoV-2 RNA in a specimen collected from the nasopharyngeal area. The identification process was carried out by applying Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) analysis, according to the guidelines outlined by the Centers for Disease Control and Prevention.

2.2. Statistical Analysis

Statistical analysis was conducted utilizing SPSS, a computerized statistical method. This approach was used to determine the probability (P-value) and chi-square (X2) statistics and to perform the t-test and ANOVA test.

Results were deemed statistically significant if the probability value exceeded 0.05, whereas results were regarded statistically significant if the P value was less than or equal to 0.05. A P value below the minimum value of 0.05 was considered to indicate statistical significance.

3. Results

The research encompassed a cohort of 250 individuals diagnosed with COVID-19, consisting of 130 men and 120 women aged 20 to 80 years. Of the sample, 68% fell into the mild/moderate category, while 80 individuals (32%) were classified as severe, as seen in the accompanying Table 1.

Table 1. Demographic characteristics of the study population N % 250

Variables	Frequency	Percentage (%)
Gender		
Male	130	52
Female	120	48
Age Groups		
20-40 Year	60	24
40-60 Year	90	36
60-80 Year	100	40
Severity of Symptoms		
Mild to Moderate	170	68
Severe	80	32

Table 2. Variables correlation with severity of symptoms

Variables	Moderate Symptoms (170)	Severe Symptoms (80)	Odd Ratio (95% Ci)	P Value
Gender				
Male	100	60	4.28 (2.37- 7.74)	<0.001*
Female	70	20		
Age Groups				
20-40a	20	20		
40-60	80	40	0.50 (0.24 - 1.03)	0.059
60-80	70	20	0.28 (0.12 - 0.63)	0.002*
40-60a	80	40		
60-80	70	20	0.75 (0.30 - 1.06)	0.07

** The P-value with statistical significance is in bold. CL – confidence interval; a is a reference*

The current study's findings revealed statistically significant variations in blood parameters, including urea, creatinine, D-dimer and blood glucose levels, within both groups under investigation.

Table 3. Estimate several blood parameters for different stages of COVID-19

Parameters	Study Groups			
	Severity	Mild To Moderate	T- Test	P= Value
Glucose (Mmol/L)	31.42± 3.42	18.69± 0.97	4.51	0.026*
S.Cr (Umol/L)	537.00± 146.30	184.70± 21.25	4.61	0.004*
Blood Ur. (Mmol/L)	19.14± 2.00	9.02± 0.35	8.55	0.002*
D.Dimer (Ng/Ml)	10750.00± 478.71	3218.00± 746.50	4.50	0.048*

**P< 0.05 significant*

The findings of our study indicate that female patients exhibited higher concentrations of blood parameters, including urea, creatinine, D-dimer, and blood glucose, compared to male patients. These differences were statistically significant at a significance level of $p<0.05$.

Table 4. Some blood parameters of the subject groups for both genders

Parameters	Patient Level Concentration Ng/Ml				P= Value
	Severe		Mild To Moderate		
	Female	Male	Female	Male	
Glucose (Mmol/L)	15.33± 4.84	17.00± 2.51	13.75± 1.06	12.00± 1.04	0.34
S.Cr (Umol/L)	500.00± 28.86	490.00± 47.25	158.25± 26.38	141.00± 11.12	<0.001*
Blood Ur. (Mmol/L)	21.08± 2/08	22.33± 0.88	16.40± 1.77	12.42± 1.55	0.011*
D.Dimer (Ng/Ml)	10333.00± 881.91	9000.00± 577.00	6166.00± 726.84	7666.00± 691.71	0.002*

**P< 0.05 significant*

4. Discussion

The clinical characteristics and outcomes of persons affected by COVID-19 are multifaceted and intricate [14]. Biochemical parameters are frequently examined as initial indicators for monitoring metabolic status and organ well-being. Surveillance of these indicators in individuals with COVID-19 is of utmost importance to obtain substantial information on the ramifications of the disease [15].

This study comprehensively analyzes the biochemical characteristics and clinical outcomes seen in patients with COVID-19 who reside in Hilla, Iraq. The laboratory value profiles of all patients were monitored. Our data analysis showed that urea, CK, and D-dimer biomarkers exhibited notable advantages in prognosticating disease outcomes. Undoubtedly, an increase in the levels of urea, CK, and, particularly, D. dimer was associated with an elevated mortality risk. Furthermore, within the scope of our investigation, it was observed that viral infection had a rapid progression in people with Chronic Kidney Disease (CKD). Similar findings have been documented in the existing literature. According to the latest updates as of April 25, 2020, the Centers for Disease Control and Prevention (CDC) have identified a higher susceptibility to severe COVID-19 infection in individuals with Chronic Kidney Disease (CKD), regardless of the specific stage of their kidney disease. According to the Centers for Disease Control and Prevention (CDC) in 2020, in an initial meta-analysis, Chronic Kidney Disease (CKD) was observed to become a notable prognostic factor for clinical outcomes associated with COVID-19 infection. This finding is noteworthy, considering that the individual studies incorporated in this meta-analysis did not establish a direct association between the outcomes of CKD and COVID-19 [16, 17].

The findings of our study indicate that male patients exhibited a higher susceptibility to experiencing a more severe deterioration in kidney function levels than female patients. This aligns with our previous observation that male sex individuals are correlated with a more severe manifestation of COVID-19 sickness and a poorer prognosis. Furthermore, a separate study revealed that male individuals constituted the majority of COVID-19 patients hospitalized at the hospital and exhibited elevated Serum Creatinine (SCr) levels [18]. "Recent literature has documented that Acute Kidney Injury (AKI) has often been observed in individuals diagnosed with COVID-19. Furthermore, the occurrence of AKI in these patients has been suggested to indicate an increased likelihood of mortality. This discovery has been described in various recent publications. Furthermore, approximately 15% of individuals diagnosed with COVID-19 have been shown to have elevated levels of Serum Creatinine (SCr) and Blood Urea Nitrogen (BUN) [5, 6].

The results of our study indicate an increase in Cr levels among individuals diagnosed with COVID-19, which is consistent with the findings reported by Deng et al. [19], who observed an increase in Cr levels among 8% of patients with COVID-19. Furthermore, a retrospective analysis of serum urea and creatinine levels in a cohort of 100 patients diagnosed with COVID-19 indicated that 35 individuals, representing 35% of the sample, exhibited elevated levels of serum urea nitrogen and creatinine [20].

The coexistence of (CKD) and (DM) sometimes manifests itself as Diabetic Kidney Disease (DKD), which can lead to increased susceptibility to severe viral infections [21]. Based on the findings of Leon-Abarca et al. [2], most individuals diagnosed with diabetic nephropathy (54.04%) experienced COVID-19 infection. Patients with only Chronic Kidney Disease (CKD) had an infection rate of 48.8%. Furthermore, among those with diabetic nephropathy who contracted SARS-CoV-2, approximately one-third developed COVID-19 pneumonia. In particular, a significant proportion of these individuals (94.22%) required hospitalization. A recent study conducted in a controlled laboratory setting demonstrated that the cytopathic effects of SARS-CoV-2 on podocytes and proximal straight tubule cells could potentially lead to the development of Acute Kidney Injury (AKI) in individuals affected by COVID-19. Pan et al. [23] reported that the highest level of ACE2 receptor expression in these cells is observed in Occidental populations. A recent study by Su et al. [22] and Jameel et al. [24] found that all patients infected with SARSCoV-2 exhibited renal structural abnormalities when evaluated by CT scans. Furthermore, kidney biopsies performed on COVID-19 patients revealed evidence of direct virus-induced damage.

Cytokine-mediated damage has been suggested as an additional mechanism of renal injury after SARS-CoV-2 infection. In the inflammatory phase of the disease, a significant proportion of patients may experience an exaggerated response called a cytokine storm, leading to unregulated pulmonary inflammation, which is believed to significantly contribute to mortality rates [25].

According to research conducted by Leon-Abarca et al. [2], it has been observed that the impact of Diabetes Mellitus (DM) on the incidence of infection, intubation, hospitalization in the ICU, and fatality of cases related to COVID-19 is more substantial compared to Chronic Kidney Disease (CKD) when considered independently. Individuals who were diagnosed with both diabetic renal disease and COVID-19 demonstrated a higher prevalence of unfavourable health outcomes and mortality compared to those who had just had chronic kidney disease and COVID-19. The data variance may be ascribed to the additional effects of chronic inflammation and immunological dysfunction. Patients with diabetic kidney disease demonstrated significantly higher rates of SARS-CoV-2 infection than persons recently diagnosed with chronic kidney disease, Intensive Care Unit (ICU) hospitalization, and mortality. The incidence of pulmonary infection and intubation in individuals with DKD was twice as high as in those with CKD alone. A separate investigation by Mohamed et al. established that chronic kidney disease was a significant autonomous indicator of mortality resulting from COVID-19, in conjunction with male gender, advanced age, and hypertension. Subsequent investigations would seek to analyze the impact of COVID-19 on enduring renal function, as elucidated by Mohamed et al. [21].

There is a growing need to conduct more research on the possible association between diabetic kidney disease and COVID-19. This is crucial to establish a comprehensive understanding of the particular mechanisms through which the virus may impact the decline in glycemic control. Acute renal injury could manifest as a result of the rapid progression of hyperglycemic hyperosmolar syndrome or diabetic ketoacidosis, as well as the advent of new cases of diabetes [25, 26]. The relationship between different vaccinations and their impact on the progression of diabetes is linked to the appearance of acute kidney injury due to the immunological response they induce, which has been demonstrated to include coagulation. Further investigation is required to gain a deeper understanding of this phenomenon.

5. Conclusion and Future Scope

The importance of biochemical indicators in COVID-19 therapy is of utmost importance, particularly in evaluating prognostic risk and illness outcomes. Alterations in these biochemical parameters indicate the progression of COVID-19 by manifesting irregularities in multiple tissues and organs. Urea, Creatine Kinase (CK) and D-dimer have been identified as the most reliable indicators to predict the severity of COVID-19 [27, 28].

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