The Relationship between The Characteristics of Type-2 DM Patients and The CKD Stage during The COVID-19 at RSI Jemursari

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ABSTRACT

Introduction: The prevalence of diabetes mellitus has risen globally, posing a substantial health challenge, with a marked increase reported in both developed and developing nations. Diabetes is a primary contributor to the global prevalence of Chronic Kidney Disease (CKD). During the pandemic, there is a considerable challenge, especially for CKD patients, including a loss in health services, vulnerability to COVID-19 infection, stressful events during social distancing, and a decrease in therapy adherence. Hence, the COVID-19 pandemic may give rise to various characteristics in individuals with chronic kidney disease.

Objective: To investigate the correlation between the characteristic of patients with type 2 diabetes mellitus and the chronic kidney disease (CKD) stage at RSI Jemursari Surabaya during the COVID-19 pandemic.

Methods: An observational analytical cross-sectional study was conducted on individuals with chronic kidney disease (CKD) previously diagnosed with diabetes mellitus (DM) during the COVID-19 pandemic from 2020 to 2022. A total of 169 samples were obtained using a simple random sampling method. The variables considered include age, gender, HbA1c, blood pressure, cardiovascular comorbidities, Pulmonary comorbidities, and history of COVID-19.

Results: The study demonstrated a significant correlation between blood pressure and kidney function tests, including blood creatine level, BUN, and eGFR, with CKD stage (P<0.05). Randomised blood glucose also has a significant correlation to the CKD stage. No notable correlation was observed among age, gender, HbA1c levels, cardiovascular comorbidities, pulmonary comorbidities, and history of COVID-19.

Conclusions: The presence of hypertension and abnormal kidney function test results correlate with the stage of chronic kidney disease (CKD) during a pandemic.

Introduction

In 2021, there were 537 million persons worldwide living with diabetes mellitus (DM). According to the International Diabetes Federation (IDF), diabetes affects approximately one-tenth of the global population. The predicted estimate for this amount is expected to rise to approximately 643 million by 2030 and 738 million by 2045. Diabetes is responsible for 6.7 million deaths, with one death occurring every 5 seconds by 2021 (IDF, 2021).

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia. This may result from impaired insulin secretion, resistance to peripheral insulin action, or a combination of both 9carillo, et al 2019). Chronic hyperglycemia, in synergy with other metabolic abnormalities in diabetic patients, can lead to damage in various organ systems, culminating in the development of debilitating and life-threatening health complications. The most prominent among these are microvascular complications (retinopathy, nephropathy, and neuropathy) and macrovascular complications that significantly increase the risk of cardiovascular diseases two to four times (Regina, et al 2022)

Approximately 50% of type 2 diabetes and a third of type 1 diabetes patients develop Chronic Kidney Disease (CKD), marked by kidney function impairment or increased urinary albumin excretion. The specific percentage of CKD attributed solely to diabetes remains unclear. Other contributors to kidney dysfunction include hypertension, dyslipidemia, obesity, vascular diseases, acute kidney injury, glomerular atherosclerosis, renal ischemia, and age-related nephron loss. Precisely defining 'Diabetic Kidney Disease' (DKD) in epidemiology or clinical practice, especially in type 2 diabetes, is challenging. Therefore, it is more accurate to identify patients with both diabetes and CKD and implement comprehensive renoprotective strategies (Thomas, et al 2015).

A previous study by Farah et al. (2021) found that diabetic kidney disease patients with an average age of 59 years exhibited correlations between older age, high triglycerides, low HDL, and increased severity of the disease. Metformin and ACEi-ARB usage showed a negative correlation with albuminuria incidence and the risk of severe CKD. The World Health Organization (WHO) notes that elderly individuals and those with pre-existing conditions like diabetes mellitus, chronic kidney disease, and heart disease are more susceptible to severe outcomes when exposed to COVID-19, with higher mortality rates (farah et al, 2021). However, the application of proven ACEi-ARB treatment for diabetic kidney disease in COVID-19 remains controversial due to

concerns about potential virus entry pathways (Abdulaziz et al, 2022). Type 2 diabetes patients experiencing diabetic kidney disease may exhibit different characteristics, especially during the COVID-19 pandemic. [MOU1] This study aims to investigate the correlation between the characteristics of patients with type 2 diabetes mellitus and the chronic kidney disease (CKD) stage at RSI Jemursari Surabaya during the COVID-19 pandemic. So that based on these data, researchers are motivated to conduct research for future purposes.

Methods

An analytical observational cross-sectional study using data from medical records was conducted on individuals with Diabetes Mellitus (DM) and Chronic Kidney Disease (CKD) between 2020 and 2022. The data collection process was conducted at RSI Jemursari Surabaya using random sampling from August to October 2023.

The study's population comprises medical data from patients with DM and CKD who went to RSI Jemursari Surabaya from 2020 to 2022. A total of 150 samples was calculated using the cross-sectional minimal sample size formula with a known population. The study variables include the patient's characteristics, namely age, gender, HbA1c levels, blood pressure level,

presence of heart disease, history of COVID-19, D-dimer values, and history of prior lung diseases. The data will undergo editing and will be provided in the form of frequency and distribution tables.

The study employed inclusion and exclusion criteria: 1. Inclusion Criteria: Patients with a confirmed diagnosis of diabetic renal illness and type 2 diabetes, aged 18 years or older, and possessing comprehensive medical record information. Exclusion Criteria: The patient needs comprehensive medical record information.

This research has been approved by the Research Ethics Committee of RSI Jemursari Surabaya Hospital No. 084/KEPK-RSISJS/V/2023. This study analyzed dependent variables using two data formats. The Pearson Chi-Square test tests demographic data if it meets the minimum test requirements. However, Kendall's test was used on categorical variables beyond 2 degrees. Age, Creatinine, urea levels, eGFR, LOS in hospital, HbA1c and RBG levels were evaluated using the ANOVA test. If data were not normally distributed, Kruskal Wallis was used.

Results

Table 1. The characteristic variable of Chronic Kidney Disease Patients in early, late and regular hemodialysis

Variable	Early stage (n=40)	Late stage (n=42)	Regular HD (n=68)	P-value
Age (year)	58,59 ± 11,07	61,13 ± 11,11	58,84 ± 11,41	0,506*
Gender (Male) – n (%)	23 (57,7)	23 (54,8)	31 (45,6)	0,813**
Blood pressure (%)				0,004***
Hypotension	3 (7,5)	6 (14,3)	7 (43,8)	
Normal	18 (45)	16 (38,1)	15 (22,1)	
Hypertension grd 1	12 (30)	11 (26,2)	17 (25)	
Hypertension grd 2	6 (15)	8 (19)	18 (26,5)	
Crisis hypertension	8 (2,5)	1 (2,4)	11 (16,2)	
COVID-19 status				0,438**
Positive result	14 (35)	12 (28,6)	16 (23,5)	
Serum Creatinin	1,53 ± 0,36	3,74 ± 1,61^{a,c}	9,14 ± 5,74^{a,b}	<0,001****
BUN	29,12 ± 12,7	60,05 ± 27,34^{a,c}	80,02 ± 37,3^{a,b}	<0,001****
eGFR	52,9 ± 16,51	19,96 ± 4,85^{a,c}	8,66 ± 3,19^{a,b}	<0,001****
Cardiovascular disease history	24 (60)	25 (59,5)	42 (61,8)	0,968**
Pulmonary disease history	22 (55)	25 (59,5)	34 (50)	0,616**
LOS in hospital (days)	6,05 ± 4,92	5,40 ± 3,7	5,16 ± 4,5	0,530****
Outcome (Death event)	5 (12,5)	14 (33,3)	15 (22,1)	0,078**

* One-Way ANOVA test
** Pearson Chi-Square test
*** Kendall's tau b test
**** Kruskal-Wallis test
Mann-Whitney test: [a] sig P<0,05 (vs Early stage), [b] sig P<0,05 (vs Late stage), [c] sig P<0,05 (vs Reguler HD).

Based on Table 1, the research findings demonstrated no significant correlation between characteristic age and gender in this study (P>0,05). COVID-19 status also has a non-significant correlation compared to the CKD stage, even during the pandemic. Also, there is no significant association between cardiovascular and pulmonary comorbidities and the stage of chronic kidney disease (CKD). Furthermore, there is no association between the length of stay and death's worst consequence. However, the study found a significant correlation between Blood pressure and kidney function tests (P<0,05).

Table 2. Characteristic of HbA1c level and Random Blood Glucose variable of Chronic Kidney Disease Patient stage

Variable	Early stage (n=29)	Late stage (n=20)	Regular HD (n=12)	P-value
HbA1c - n (%)				
<7	8 (27,9)	7 (35,0)	4 (33,3)	0,540*
7-9	12 (41,4)	5 (25)	2 (16,7)	
>9	9 (31,0)	8 (40)	6 (50)	
RBG	210 ± 91	276 ± 126	159 ± 86[a]	0,041**

* Kendall's tau-b test
** Kruskall-Wallis test
Mann-Whitney: [a] sig P<0,05 (vs Late stage)

Based on Tabel. 2, the research findings demonstrated no significant correlation between characteristic HbA1c and CKD stage in this study. However, the study found a significant correlation between random blood glucose levels and CKD stage during admission.

Discussion

The COVID-19 pandemic has caused significant effects, particularly on individuals with chronic kidney disease (CKD). Prior studies have demonstrated that the COVID-19 pandemic has both direct and indirect impacts on the quality of life of individuals with chronic kidney disease (CKD). Chronic Kidney Disease has been identified as a separate risk factor for the illness and death caused by COVID-19. Multiple investigations have consistently linked kidney comorbidities with disastrous outcomes of COVID-19 (Sidorenkov et al, 2014).

The study demonstrates that individuals with hypertension are associated with advanced CKD stages. The serum creatinine and blood urea nitrogen (BUN) levels have experienced a notable rise, especially in Regular HD patients and in the late stage compared to the early stage. The study also shows a significant relationship between BUN and serum Creatinine in the CKD stage, according to this study. However, there is no significant relationship between other variables,e.g. age, gender, COVID-19 status, and Cardiovascular and pulmonary disease history. Our study also found no correlation between length of stay (LOS) in hospital and worst outcome between CKD stage groups. This finding proves that CKD stage characteristics may differ greatly if compared between stages, except for Blood pressure variables and kidney function test abnormalities, e.g. BUN, Serum Creatinine and eGFR.

Previous study data (Diamantidis et al, 2023, Mohamed et al, 2021) between the pandemic periods showed a different result: age and gender characteristics show a relationship with the CKD state but not the CKD stage. In contrast to our work, many studies have attempted to compare the CKD and Non-CKD groups, but not specifically

the different stages of CKD. According to COVID-19 status in CKD patients, a previous study (Diamantidis et al, 2023) also showed that COVID-19 infection worsened the stage of CKD and rapid kidney function decline. Unlike our study, no relation occurred between the CKD stage groups.

The difference in results between the two studies could be attributed to the disparity between the populations and methodologies employed in the research.

Furthermore, our investigation revealed a potential correlation between blood pressure levels and chronic kidney disease (CKD) stage during the pandemic. Hypertension is recognized as associated with CKD and is responsible for developing interstitial fibrosis and tubular atrophy (Mathew et al, 2023). Advanced chronic kidney disease (with an estimated glomerular filtration rate of 30 mL/min/1.73 m2) is marked by impaired endothelium functioning, and these endothelial layer changes are closely associated with hypertension (Haruhara et al, 2015). However, chronic kidney disease (CKD) also contributes to an elevated rate of arterial stiffness, which in turn leads to hypertension. The most detrimental outcome occurs when hypertension leads to an increase in oxidative metabolism, which is related to renal hypoxia and contributes to raised blood pressure and the

advancement of chronic kidney disease (CKD) (13). COVID-19 also has a role in a decrease in patient hypertension therapy adherence (Dhaun et al, 2006) and medical care for and self-management of chronic hypertension (Fine et al, 2008), resulting in uncontrolled blood pressure.

Cardiovascular and pulmonary comorbidities are strongly associated with the severity and mortality of COVID-19 (Rahman et al, 2021). However, its correlation with the CKD stage remains unclear, especially during the pandemic. According to Li et al. (2014), patients with cardiovascular comorbidity do not correlate with the stages of CKD except in the dialysis group. The result may differ from our study because of the number of patients and the different conditions between the pandemic and the non-pandemic state. As previously mentioned, the pandemic plays a role in increasing cardiovascular comorbidity in every stage of CKD and contributing to cardiovascular events during the pandemic (Gotanda et al, 2022). Two common pulmonary comorbidities are COPD (Lie at al, 2014) and Asthma (Honardoos et al, 2021). A previous study by (Lie at al, 2014) demonstrated that COPD decreases renal filtration function based on blood creatinine results but not Urea levels. However, COPD alone does not significantly decrease GFR unless it is accompanied by concomitant hypertension.

However, it is difficult to assume that pulmonary history can cause reduced kidney function unless accompanied by additional variables such as sepsis and others.

The study also found that CKD stages did not increase the length of stay in the hospital and the worse outcome. However, during a pandemic, mostly CKD is accompanied by primary diseases that worsen kidney function, such as COVID-19. Our closed analysis showed that COVID-19 infection with CKD has a longer length of stay and worse outcomes when compared to CKD without COVID-19 infection. Previous studies (Gok et all, 2021, Boiko et all, 2022) have shown a linear result. The study also showed significant mortality and more hospitalization duration in comparison between early CKD and late CKD with COVID-19. In conclusion, our study only compared the CKD stage during the pandemic without COVID-19 status, so our comparison of early and late CKD stages and regulator HD patients was non-significant.

Our study also examined the correlation between HbA1c and random blood glucose levels to explain the fluctuation level during the pandemic according to the CKD stage. The study demonstrated no significant correlation between HbA1c and RBG levels according to the CKD stage. A previous study (Kuo et al, 2016), but not in pandemic situations, demonstrated that the only positive correlation between HbA1c and eGFR exists in stage 5 CKD. However, The prognostic role of HbA1c in patients with stage 5 CKD was unclear because of impaired glucose metabolism in advanced CKD, and the HbA1c level may be altered by anemia or erythropoiesis-stimulating agent use (Mak, 2000). According to a study, there was a decrease in HD patients during the pandemic, a primary reason for fears of COVID-19 (Sultan et al, 2022). Therefore, it is challenging to generalize non-significant results in HbA1c and RGB levels during the pandemic due to a limited number of patients.

Conclusion

There is a correlation between the presence of hypertension and abnormal kidney function tests with the stage of chronic kidney disease (CKD) during a pandemic. The study also notes if there is a correlation between random blood glucose levels according to CKD stage. It is recommended that type 2 DM patients with CKD continue to be carefully monitored and managed during this pandemic. Strict preventive measures and interdisciplinary collaboration must be improved to reduce the risk of more severe complications in these patients. Emphasis on patient education regarding holistic disease

management is also essential to minimize possible adverse effects.

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