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HbA1c AS Early Warning Complications Of Kidney Failure In Type 2 Diabetes Mellitus

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Abstract :

Chronic kidney disease (CKD) is closely related to diabetes. Basic information about the treatment and physical condition of diabetic patients should be analyzed to provide further evidence of prevention. Based on the high prevalence of DM among patients with renal failure, there is a great need to learn more about its prevention and management including laboratory diagnostic tests because HbA1c levels are directly proportional to blood glucose levels.

The purpose of this study was to determine the effect of HbA1C levels on creatinine levels in patients with type 2 diabetes mellitus This type of research is a quantitative study with a cross-sectional approach. The sample in this study was 38 DM patients who had their diagnosis confirmed by using consecutive sampling techniques. The respondent's blood sample was taken at the respondent's house according to the data from the health care center and the HbA1c and creatinine levels were tested in the laboratory. Data analysis to determine how much risk HbA1c levels can cause kidney failure using the chi-square test. The results of this study indicate that there is no relationship between HbA1C levels and the incidence of kidney failure with a p-value of 0.588, OR 0.658. this research showed that there was no relationship between HbA1C levels with the incidence of kidney failure.

Keywords: Diabetes mellitus; Chronic kidney disease; ERSD; creatinine; HbA1C

INTRODUCTION :

Diabetes mellitus (DM) ranks high on the international health agenda as a global pandemic and as a threat to human health and the global economy. The International Diabetes Federation (IDF), Diabetes Atlas, shows that there are 425 million people with DM, reflecting a prevalence rate of 8.6% in adults. DM conditions vary from country to country around the world (Abate et al., 2021). Meanwhile in Indonesia based on Riskesdas 2018, the prevalence of Diabetes Mellitus (DM) from 6.9 percent in 2013 increased to 8.5 percent, in 2018. That means, there are 22.9 million Indonesians who suffer from DM (Health Research and Development Agency). RI, 2018).

There are many complications of DM, such as diabetic retinopathy and diabetic nephropathy, which can lead to blindness and kidney failure. In addition, DM increases the risk of cardiovascular disease and death leading to high expenditure. Studies have shown that the gloomy situation regarding DM can be reduced through proper management and education (Ackermann et al., 2019).

Adequate glycemic control can significantly lower the risk of DM-related complications, leading to delays in disease progression. National public health management for DM needs to be initiated immediately to delay the development of DM. However, basic information about the treatment and physical condition of diabetic patients should be analyzed to provide further evidence of prevention (ADA, 2020).

Type 1 diabetes is mainly caused by autoimmune-mediated destruction of pancreatic beta cells leading to insulin deficiency. This is usually accompanied by changes in lipid metabolism, increased hyperglycemia-mediated oxidative stress, endothelial cell dysfunction, and apoptosis. Similarly, in type

2 diabetes, increased glucotoxicity, lipotoxicity, endoplasmic reticulum stress, and apoptosis lead to progressive loss of beta cells (Ahmed et al., 2016).

While type 1 diabetes is characterized by the presence of beta-cell autoantibodies, the combination of peripheral insulin resistance and dysfunctional insulin secretion by pancreatic beta cells is involved in the pathogenesis of type 2 diabetes. Many pathophysiological factors are involved in insulin resistance. Although the exact nature of these factors is not fully understood, it is widely accepted that oxidative stress, inflammation, and other genetic, behavioral, environmental, and epigenetic factors play an important role (Bekele et al., 2020).

Patients with diabetes mellitus associated with renal impairment have an increased risk of death, especially a higher risk of cardiovascular death, when compared to other diabetic patients without renal impairment (Akila et al., 2021). In the early stages of renal failure, insulin secretion and resistance in peripheral tissues, especially in skeletal muscle, is reduced, and in the advanced stages of renal failure, renal clearance is reduced. These facts are clinically important in the treatment of diabetes. Based on the high prevalence of DM among patients with renal failure, there is a great need to learn more about its prevention and management including laboratory diagnostic tests.

Chronic kidney disease (CKD), especially CKD associated with diabetes. Diabetes remains the leading cause of the end-stage renal disease (ESRD) in most countries in the world, accounting for 40-50% of the incidence of ESRD cases. To prevent ESRD in individuals with diabetes, we must first carry out adequate screening and detect CKD. Unfortunately, the enormous burden of CKD remains undetected among adults with diabetes. Screening programs are generally aimed at conditions with a substantial public health impact and benefit from early intervention (Cheng et al., 2021)

Kidney function, in a broad sense, as a filter. Renal function has traditionally been assessed using serum creatinine, a muscle metabolite that is filtered and freely excreted by the kidneys. However, baseline serum creatinine reflects a person's muscle mass (Yun et al., 2021).

Thus, the same creatinine value may reflect different levels of renal function in young and muscular individuals than in frail older people. To address this variability in creatinine formation, equations for estimating GFR have been developed that use serum creatinine but also include other variables that affect muscle mass and creatinine. Repeated determination and establishment of trends over time may be the key to understanding renal function in individuals with diabetes (Kebede et al., 2021)

The ADA has recently recommended an HbA1c with a cut-point of 6.5% for diagnosing diabetes as an alternative to the fasting plasma glucose-based criteria (FPG 7.0 mmol/L). Glucose-bound (glycated) hemoglobin or HbA1c provides the average level of glucose in a person's blood when glycated with hemoglobin. It is important to note that HbA1c levels are directly proportional to blood glucose levels (ADA, 2020).

Seeing the traditional function of creatinine is as an indicator of a person's muscle mass and can be freely excreted through the kidneys. However, in early diabetes mellitus patients, there has not been a decrease in muscle mass which causes an increase in serum creatinine. In addition, creatinine must involve other variables that affect muscle mass to estimate GFR in renal failure patients. Therefore, we are interested in testing other laboratory tests in predicting the risk of kidney failure in DM patients, namely by using HbA1c which is a sign of DM. Based on the described background, the research problem

can be formulated "Can HbA1c be an early warning of the risk of kidney failure in patients with Type 2 Diabetes Mellitus".

MATERIAL & METHODS :

This type of research is a quantitative study with a cross-sectional approach that aims to determine the relationship between creatinine and HbA1c laboratory tests in predicting the risk of kidney failure in DM patients. The sample in this study was 38 DM patients whose diagnosis had been confirmed by using consecutive sampling techniques. The respondent's blood sample was taken at the respondent's house according to the data from the health care center and the HbA1c and creatinine levels were tested in the laboratory. Data analysis to find out how much risk HbA1c levels can cause kidney failure using the chi-square test.

RESULTS :

a. Respondent characteristics

The characteristics of respondents in this study included age, gender, duration of type 2 diabetes mellitus, occupation, history of drug consumption, HbA1C values , and creatinine values, as shown in the table 1.

Table.1 The characteristics of respondents

No	Variable	Result*
1	Age (years)	44 ±8.9
2	Gender (%)	
	Man	23 (60.5)
	woman	15 (39.5)
3	Work (%)	
	Not Working/housewife	10 (26.3)
	Businessman	6 (15.8)
	Private sector employee	13 (34.2)
	retired	1 (2.6)
	soldier/police/civil servant	8 (21.1)
4	History of Drug Consumption (%)	
	yes	15 (39.5)
	no	23 (60.5)
5	DM history	7.29±3.1
6	creatinine	1.02±0.239
7	HbA1C	8.3±2.7
8.	HbA1C (%)	
	Normal	14 (36.8)
	High	24 (63.2)
9.	creatinine (%)	
	Normal	29 (36.8)
	High	9 (63.2)

*Data is presented as a percentage for categorical variables and mean (±) standard deviation for continuous variables.

Based on table 1 above, it was found that the respondents in this study were men with an average age of 44 years who worked as private employees. The average history of suffering from diabetes mellitus is 7.29 years but does not take regular drugs. The average HbA1C level was 8.3 and creatinine 1.02

b. Effect of HbA1C on creatinine

Table 2. Effect of HbA1C on creatinine

		Creatinine			P-value	OR	Upper	Lower
		Normal	High	Total				
HbA1C	Normal	10 (26.3%)	4(10.5%)	14 (36.8%)	0.588	0.658	0.144	3.013
	High	19(50%)	5(13.2%)	24(63.2%)				
	Total	29(76.3%)	9(23.7%)	38(100%)				

Based on table 4.4 above, it was found that 13.2% of respondents who had high HbA1C levels also had high creatinine levels. The results of this study indicate that there is no relationship between HbA1C levels and the incidence of kidney failure. However, it can be predicted that DM patients who have high HbA1C levels can experience kidney failure up to 3 times.

DISCUSSION :

This study provides evidence to conclude that HbA1c may not yet be a useful biomarker to identify individuals at risk for renal impairment in the general population. Since a high prevalence of non-communicable disease risk factors has recently been reported in the population, these findings may be important for implementing prophylactic interventions to prevent or delay the incidence of renal failure. Previous studies have reported that high HbA1c values can be a strong predictor of all-cause mortality in populations with and without diabetes. In addition, poor glycemic control, as evidenced by high HbA1c levels, is associated with the incidence of CKD in patients with diabetes, even in the absence of albuminuria and retinopathy. However, the association between HbA1c concentrations and the presence of CKD in the general population, regardless of diabetes status, has only been studied by a small number of people.

In our study, we looked at the risk between HbA1 concentrations and CKD. This risk was independent of the common factors associated with CKD, including diabetes status. Therefore, it is plausible that this clinical appearance appears to be mediated by HbA1c levels. In other words, the degree of hyperglycemia, regardless of the presence or absence of diabetes, may be associated with the future incidence of renal failure. High HbA1c levels in respondents can predict a higher probability which is indicated by high creatinine levels (13.2%). Further prospective studies are needed to clarify this issue.

Moreover, Given that the upper limit of HbA1c in this patient was 6.4%, we cannot rule out that prediabetes status could be negatively impacted in our study. The fact that an increased prevalence of metabolic risk factors is strongly associated with a higher prevalence of CKD in the general population

supports this hypothesis (de Bhailís et al., 2021). Whatever the case, whether lowering HbA1c levels can decrease the incidence of renal failure in this high-risk population is worthy of investigation by clinical trials.

A mechanistic relationship between the incidence of renal failure can be established in these patients. Very likely, insulin resistance factors and several risk factors may be associated with CKD in the general population. Increasing evidence suggests that pathophysiologically, there are toxic effects of glucose fluctuations. The glycemic situation has been found to be proatherogenic through chronic inflammation (Wu et al., 2021). Furthermore, HbA1c may be a link between chronic hyperglycemia and oxidative stress, and endothelial dysfunction. HbA1c is a target for intracellular glycoxidation and peroxidation reactions that result in the formation of advanced glycation end products (Bakris et al., 2020; Bomholt et al., 2021; Budury & Khamida, 2021, p. 19; Supriyadi et al., 2021; Walbaum et al., al., 2021), which are involved in the initiation and progression of atherosclerosis. Finally, changes in glycemia can induce growth factor activation, which may contribute to the development of intraglomerular hypertension in people with prediabetes.

This study has several limitations. The cross-sectional study design did not allow us to elucidate the temporal direction of the observed association between HbA1c and CKD, or risk of exposure, which would be better evaluated by a longitudinal study. Thus, whether HbA1c concentrations and CKD are causally related cannot be inferred from this cross-sectional study. In addition, the prevalence rate of CKD seen in this study was low.

However, our study involved a random and representative sample of the adult population. Future longitudinal studies stemming from this study should clarify this point. Second, the population studied was not exclusively; thus, the results can be extrapolated to other populations with the same diet or lifestyle. Finally, we performed only a single blood extraction for the diagnosis of diabetes based on the glycemic index.

CONCLUSION :

This community-based epidemiological study highlights the independent association between HbA1c levels and CKD regardless of diabetes status. A very small increase in mean HbA1c level could significantly influence the incidence of future renal failure events in longitudinal studies. However, HbA1c examination cannot be said to be the gold standard in predicting the condition of kidney failure in DM patients due to various factors such as the cost of HbA1C examination which is more expensive than creatinine examination, and the availability of examination reagents.

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