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To Study the Potential Biomarkers for the Early Identification of DKD in Vidharbha Region

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ABSTRACT

Diabetic nephropathy is another name for diabetic kidney disease (DKD). Diabetes-related kidney disease is referred to as DKD. It alters the normal process of removing waste products and excess fluid from the body by affecting kidney function. In India, diabetic kidney disease (DKD) is more common. One of the key reasons for the increase in new cases is that DKD patients are often undiagnosed and untreated. A diagnostic marker that can detect a disease at an early stage can be an effective tool for slowing disease development and avoiding the worst disease-related outcomes. Investigate the factors that influence renal function and patient outcomes in DK disease. The study was carried out by the Department of Biochemistry at Nagpur's Datta Meghe Medical College. A total of 300 people participated in the study, including 150 healthy controls and other study group contain 150 DKD patients. The subjects were divided into three categories: normo-albuminuria, micro-albuminuria, and macro-albuminuria. In each family, there are 50 patients. Biochemical markers such as HbA1c, Urea, Creatinine, uric acid, protein, Total Cholesterol, Triglyceride, eGFR, and UACR were measured using specific biochemical procedures. The goal of this study was to see if galectin-3 and GDF-15 may be used as a biomarker in the early identification of DKD. The research was conducted at Nagpur's Datta Meghe Medical College's Department of Biochemistry. A total of 300 people took part in the study, 150 of whom were safe controls and 150 of whom were DKD patients. The subjects were divided into three categories: normoalbuminuria, microalbuminuria, and macroalbuminuria. There are 50 patients in each home. Specific biochemical procedures were used to measure biochemical markers such as HbA1c, Urea, Creatinine, uric acid, protein, Total Cholesterol, Triglyceride, eGFR, and UACR. The researchers wanted to determine if galectin-3 and GDF-15 could be used as a biomarker for DKD early identification. To validate galectin-3 and GDF-15's potential as a potential predictive marker for use in routine clinical practice, multi-center, multi-national, and multi-ethnic studies are needed. Future research is also needed to assess CKD awareness in a large community-based sample and establish a CKD awareness model for both elevated patients and the general community in order to promote early detection, better treatment, and creative care. To generalise the finding of anaemia in DKD patients, we also suggest broad epidemiological studies with a comparable control group.

KEY WORDS: T2DM, GDF-15, CKD, DKD, UACR, EGFR, HBA1C.

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INTRODUCTION

Diabetic nephropathy, also known as diabetes kidney disease (DKD), is a common diabetic consequence. DKD is marked by a decrease in glomerular filtration rate or an increase in urine albumin excretion rate, or both (Amin, A. P et al., 2013). It is one of the most prevalent T2DM

problems, affecting roughly 20% to 40% of diabetic individuals (Rakesh Kumar et al., 2020). End-stage renal failures are also caused by diabetes and hypertension, which account for almost half of all cases (Lea, J. P et al., 2002)

DKD is more common in India; according to a population-based epidemiological survey, about 40% of Indian T2DM patients have CKD (Prasannakumar, M et al., 2015). Similarly, one out of every five hypertensive people has CKD. Diabetes and chronic kidney disease were ranked 9th and 18th in the 2010 Global Burden of Disease report, respectively, in terms of total number of deaths worldwide.

Early detection can halt or even reverse the progression of kidney damage. Despite this, the majority of cases of CKD go undetected for years. Early diagnosis and prevention of disease progression in high-risk individuals are hampered by a lack of information about the disease and the lack of possible biomarkers. Uric acid and urinary creatinine is a risk factor for DKD. It's regarded to be a modifiable risk factor for kidney disease progression and an independent risk factor for cardiovascular events.

In published investigations, galectin-3 and growth differentiation factor-15 (GDF-15) have been linked to renal disease. Endothelial cells, epithelial cells, and macrophages all have galectin-3, a -galactoside–binding protein. It plays a role in immunity, inflammation, and cancer control and is highly expressed in monocytes. Growth differentiation factor-15 (GDF-15), also known as macrophage inhibitory cytokine, is a member of the transforming growth factor superfamily..10 According to the literature, GDF-15 has recently been discovered to be a useful biomarker for predicting cardiovascular death, preoperative myocardial injury, acute renal injury after cardiac bypass surgery, CKD mortality, and colorectal cancer specific mortality.

Anemia, depression, cognitive impairment, and other complications have been attributed to DKD patients. Weak diabetes-related self-care habits, poor sleep quality, poor fitness, poor drug adherence, poorer glycemic control, and increased diabetic complications are all caused by anaemia, depression, and cognitive impairment. In people with diabetes, depression and anaemia as a co-morbid disorder are also responsible for increased impairment, morbidity, mortality, and a significant health economic burden on both the patient and the health-care system. A person with T2DM benefit from early diagnosis and treatment because it improves their quality of life, prevents or delays complications, and improves glycemic regulation. Since there is little evidence in DKD patients, it is important to consider the frequency and correlates of comorbid conditions. As a result, the aim of this study was to find possible biomarkers for the early detection of DKD and other disease-related outcomes.

MATERIAL AND METHODS

The research was done at Nagpur's Datta Meghe Medical College's Department of Biochemistry. The research enrolled 300 participants, 150 of whom were healthy controls and 150 of whom were DKD patients. Normoalbuminuria, microalbuminuria, and macroalbuminuria were the three categories for the participants. From existing families, age-matched stable controls were chosen. Prior to the start of the study, the patients' informed consent was obtained. A proforma is a form that gathers details about a patient's clinical background as well as prior inquiries into their disorders.

Place of Study: The research was carried out in collaboration with SMHRC Hospital, Wardha, at the Department of Biochemistry, Datta Meghe Medical College and SMHRC Hospital, Deemed University, Nagpur.

Sample Collection: Venipuncture in clean test tubes was used to extract blood samples after a 12-hour overnight fast. The samples were centrifuged at 2500 rpm for 15 minutes, and serum aliquots were held at minus 20 °C for a period of four weeks.

METHODOLOGY

1. The HbA1c test was carried out using a BIORAD testing system and a fully automated HPLC.
2. A updated Jaffe colorimetric procedure was used to calculate serum creatinine using a fully automated Siemens adiva-1800 chemistry analyzer.
3. Blood glucose levels were calculated using a fully automated Roche Cobas 6000 analyzer.
4. An enzyme-linked immunosorbant assay for measuring human Galectin-3 in plasma samples.
5. This is an enzyme-linked immunosorbant assay for measuring human GDF-15 in serum, plasma, and cell culture supernatants in a quantitative manner..

RESULTS

According to Table 1, there was no significant difference in serum uric acid, serum protein, total cholesterol, or triglyceride in any of the three classes. The classes differed considerably in HbA1c, eGFR, serum creatinine, albumin, urea, and UACR.

T2DM patients with macroalbuminuria exhibited significantly greater galectin-3 levels than T2DM patients with microalbuminuria or normoalbuminuria, as seen in Table 2. In T2DM patients with macroalbuminuria and microalbuminuria, GDF-15 levels were significantly higher than in T2DM patients with normoalbuminuria. Patients with poor renal function had greater levels of galectin-3 and GDF-15. Galectin-3 and GDF-15 levels are higher in DKD patients who are classified by albuminuria and eGFR. Patients with macro-albuminuria had higher levels of galectin-3 than those with micro-albuminuria or normo-albuminuria. Galectin-3 levels were found to be related to serum creatinine, UACR, and triglycerides. Galectin-3 biomarkers, on the other hand, had a negative relationship with eGFR. GDF-15 levels were also observed

to have a favorable relationship with urea, creatinine, uric acid, and UACR. GDF-15 and eGFR levels were discovered to have a negative relationship.

DISCUSSION

In recent decades, the prevalence of CKD has risen sharply. CKD affects approximately 40% of T2DM patients in India. 4,8 Chronic kidney diseases (CKD) have a wide range of causes, all of which are characterised by a decrease in eGFR over time, albuminuria, or both. 2 Evidence from epidemiological research suggests that if CKD is detected early on, it can be prevented and reversed before it progresses to ESRD. 13 Early detection and treatment are the best cost-effective and public-health techniques for dealing with CKD. As a result, the first goal of this study was to investigate galectin-3 and GDF-15's diagnostic potential in the early diagnosis of CKD. According to the findings of this study, both galectin-3 and GDF-15 levels were considerably higher in T2DM patients with CKD. Patients with greater galectin-3 levels had a higher chance of developing CKD, according to O'Seaghdha et al.201315. In their work, Tang et al., 201116 identified a negative relationship between galectin-3 levels and eGFR. Lajer et al., 201017 identified an inverse connection between eGFR and GDF-15 in T1DM patients with nephropathy. It was associated with a quick decline in eGFR and an increased risk of ESRD development.

Early detection and treatment are the best cost-effective and public-health techniques for dealing with CKD. As a result, our third goal was to evaluate CKD awareness among high-risk individuals with diabetes and hypertension as co-morbid conditions. The current research found that these patients had no knowledge of CKD. Just about a fifth of the patients have a thorough understanding of CKD. Other research conducted around the world has revealed a lack of understanding of CKD. Chow et al 2014.18 Depressed T2DM patients have a higher risk of complications, according to our findings. Our results matched those of Black et al., 200319, who concluded that depression was significantly associated with increased microvascular and macrovascular complications in T2DM patients. Many studies from Global Burden of Diseases20,21 reflect the effects of diabetes on health. A number of studies reflected on kidney related problems 22-25. Related studies on diabetes were reviewed26-28.

Table 1. Patients with normoalbuminuria, microalbuminuria, and macroalbuminuria have different levels of biochemical parameters.

Parameters	T2DM with Normo-albuminuria Group I (mean±SD)	T2DM with Micro -albuminuria Group II (mean ±SD)	T2DM with Macro -albuminuria Group III (mean ±SD)
HbA1c (%)	7.11±0.85	8.9±2.45	9.9±1.95
Blood urea (mg/dl)	29.6±13.6	40.5±19.25	38.6±18.96
Creatinine(mg/dl)	1.0±0.43	1.8±0.89	1.9±0.94
Uric acid (mg/dl)	5.9±2.44	6.0±2.48	5.6±31
Serum protein total (g/dl)	7.9±0.70	7.8±0.68	7.7±0.52
Total Cholesterol (mg/dl)	180.5±55.07	168.8±43.1	187.8±57.2
Triglyceride (mg/dl)	150.2±90.52	161.7±94.3	164.5±98.7
eGFR (mL/min/1.73 m2)	87.0±31.41	68.7±32.20	69.1±34.69
UACR (mg/g)	22.6±5.32	148.8±52.17	350.5±43.5

Table 2. Shows the plasma levels of Galectin-3 and GDF-15 in the different study groups

Parameters	T2DM with Normo-albuminuria Group I (mean ±SD)	T2DM with Micro -albuminuria Group II (mean ±SD)	T2DM with Macro -albuminuria Group III (mean ±SD)
Galectin-3 (ng/ml)	8.9±9.21	10.4±9.40	18.5±13.9
GDF-15 (pg/ml)	860±475.12	1158.3±528.23	1378.7±674.98

We feel that more epidemiological study using real-world data from diabetic patients would help to validate the prevalence of depression in diabetic patients. Furthermore, large epidemiological studies with a comparable control group, focused on metrics like glycated haemoglobin, fasting plasma glucose, and

diabetes duration, can benefit in the examination of T2DM's link with depression as a risk factor.

CONCLUSION

In this study, galectin-3 and GDF-15 were discovered as diagnostic predictors for the early recognition of DKD. The findings of this study will be useful in framing a CKD awareness model for high-risk patients. Anemia and depression screening should be performed on a regular basis to avoid CKD development and diabetes complications. In India, a diabetes treatment programme can include depression screening at an early stage.

Multicenter, multinational, and multiethnic studies are required to validate galectin-3 and GDF-15's as a potential predictive marker for use in routine clinical practise. Future research is also needed to evaluate CKD knowledge in a broad population-based sample and to develop a CKD awareness model for both high-risk patients and the general population in order to encourage early detection, improved treatment, and creative care. To generalise the finding of anaemia in DKD patients, we also suggest broad epidemiological studies with a comparable control group.

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