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ASSESSMENT OF THE IMPACT OF VITAMIN D SUPPLEMENTATION ON PROTEINURIA IN INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS

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Abstract:
Background: Type 2 Diabetes Mellitus (T2DM) is a prevalent metabolic disorder associated with various complications, including proteinuria, which is a key indicator of renal dysfunction.

Aim: The main goal of this research is to assess whether Vitamin D supplementation can effectively mitigate proteinuria in patients diagnosed with T2DM. The research seeks to elucidate potential role of Vitamin D in ameliorating renal complications and improving overall kidney health in this patient population.

Place of Study: The first Affiliated Hospital Of Xinjiang Medical university.

Methods: A randomized controlled trial conducted involving individuals diagnosed with T2DM and exhibiting proteinuria. Individuals randomized at random to the intervention group, who get Vitamin D supplements, and the control group, who receive a placebo. A total of 150 individuals with type 2 Diabetes Mellitus recruited from the outpatient department of the First Affiliated Hospital of Xinjiang Medical University. The intervention group receive a specified dose of Vitamin D for a predetermined duration. UACR measured at baseline and regularly during the study period to assess changes in proteinuria. SPSS 24.0 was used to analyze all data.

Results: The gender distribution was 53.3% males and 46.7% females. The mean age of the participants was 52.4 ± 7.8years. The mean Body Mass Index (BMI) was 29.1 ± 3.4 kg/m² and the average diabetes duration 6.2 ± 2.1. Preliminary data presented, including the average alteration in UACR levels, providing insights into effect of Vitamin D supplementation on proteinuria in individuals with T2DM.

Conclusion: In this study, the influence of Vitamin D supplementation on proteinuria in individuals with type 2 Diabetes Mellitus, with a focus on the average alteration in urinary albumin/creatinine ratio (UACR), suggests a potential positive effect. While additional research is warranted to establish a definitive link, preliminary findings indicate that Vitamin D supplementation may contribute to mitigating proteinuria in this population.

Keywords: Type 2 Diabetes Mellitus, Vitamin D supplementation, proteinuria, urinary albumin/creatinine ratio (UACR), randomized controlled trial, renal complications.

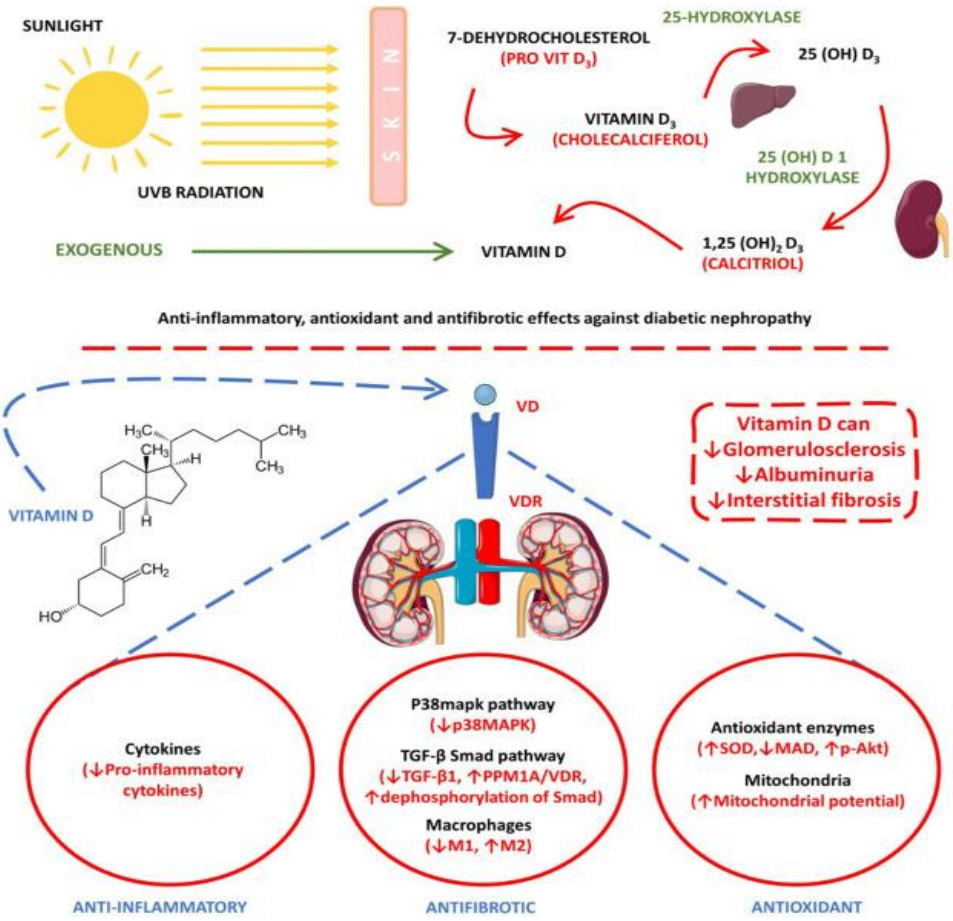
INTRODUCTION:

T2DM is a chronic metabolic condition characterized by insulin resistance and relative insulin insufficiency, manifesting in high blood glucose levels [1]. It represents a significant global health challenge with escalating prevalence rates. One of the complications associated with T2DM is diabetic nephropathy, a progressive kidney disease that manifests as proteinuria, a condition marked by increased urinary excretion of proteins, primarily albumin [2]. The urinary albumin/creatinine ratio (UACR) serves as a reliable biomarker for assessing proteinuria and is commonly utilized in clinical settings to monitor kidney function in individuals with diabetes [3].

Vitamin D, a fat-soluble secosteroid, is essential for maintaining bone health, immune function, and calcium homeostasis. Recent research has also suggested a potential link among Vitamin D deficiency and the progression of diabetic nephropathy [4]. This has led to growing interest in exploring the impact of Vitamin D supplementation on proteinuria in patients with T2DM, with a focus on its effect on the UACR [5]. Understanding association among Vitamin D status and proteinuria could provide valuable insights into novel therapeutic approaches for managing diabetic nephropathy and improving renal outcomes in this high-risk population [6].

Numerous research studies have demonstrated that Vitamin D receptors are present in the kidneys, suggesting a direct role of Vitamin D in renal function. Additionally, Vitamin D has anti-inflammatory and anti-fibrotic properties, which may contribute to its potential renoprotective effects [7]. In the context of T2DM, where inflammation and oxidative stress play pivotal roles in expansion and progression of diabetic nephropathy, Vitamin D supplementation could emerge as a promising intervention to mitigate these pathological processes [8].

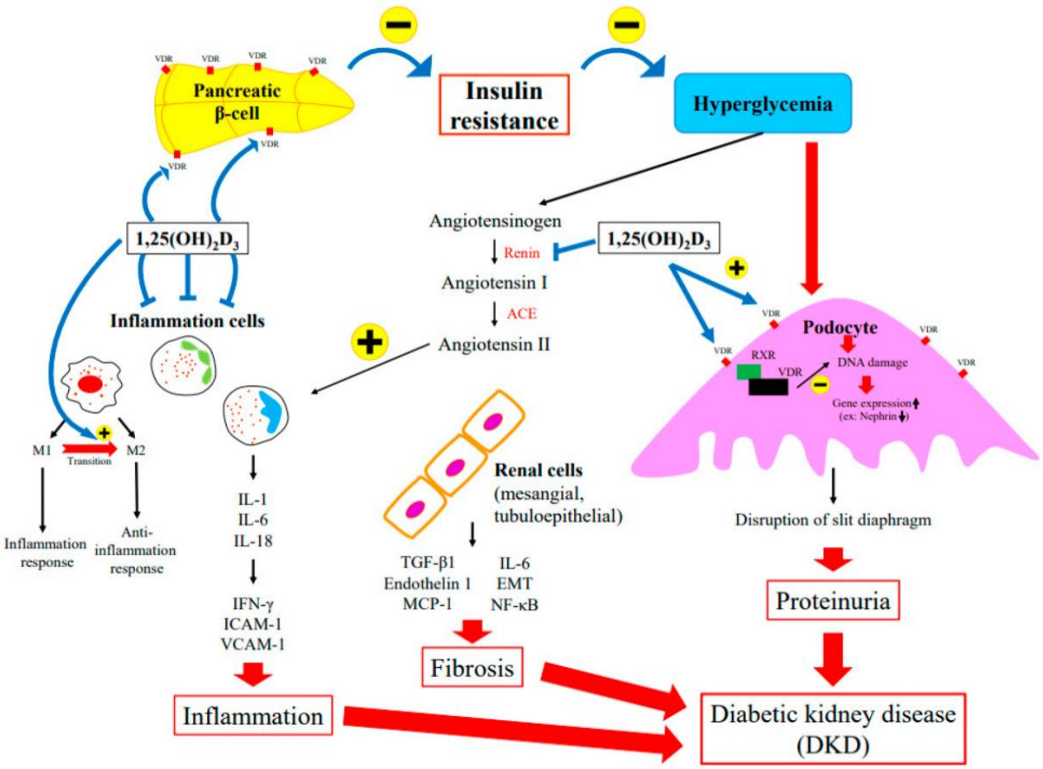
Image 1:



The link between Vitamin D deficiency and increased proteinuria were observed in various populations, including those with diabetes. Furthermore, research using observations have found an inverse relationship among blood Vitamin D levels and the UACR, suggesting that those with poor Vitamin D status are more likely to develop proteinuria [9]. However, the evidence from interventional studies investigating effect of Vitamin D supplementation on proteinuria in T2DM remains inconclusive and warrants further exploration [10].

The rationale for exploring association among Vitamin D and proteinuria in T2DM extends beyond its potential renal benefits. Given the well-established association between proteinuria and cardiovascular morbidity and mortality, addressing proteinuria in individuals with T2DM may have broader implications for cardiovascular health [11]. Understanding whether Vitamin D supplementation can effectively reduce proteinuria in this population could have profound implications for clinical practice and public health strategies [12].

Image 2:



This study aims to systematically review and analyze present literature on effect of Vitamin D supplementation on proteinuria in individuals with T2DM, with a specific focus on changes in the UACR [13]. By synthesizing available evidence, this research seeks to elucidate the potential benefits and limitations of Vitamin D supplementation as an adjunctive therapeutic approach for managing proteinuria in T2DM. The findings from this study may inform medical guidelines and contribute to development of targeted interventions aimed at improving renal and cardiovascular results in individuals having T2DM and proteinuria [14].

METHODOLOGY:

Study Design:

The research employ a randomized controlled trial (RCT) design. Participants randomly assigned to the intervention group receiving Vitamin D supplementation and the control group receiving a placebo. This design helps ensure a rigorous assessment of the impact of Vitamin D on proteinuria in individuals with type 2 Diabetes Mellitus (T2DM).

Participants Selection:
A total of 150 individuals with type 2 Diabetes Mellitus recruited from the outpatient department of First Affiliated Hospital of Xinjiang Medical University. Inclusion criteria involve individuals aged 30-70 years, diagnosed with T2DM for at least one year, and exhibiting proteinuria. Exclusion criteria include individuals with chronic kidney disease, other metabolic bone disorders, or those currently on Vitamin D supplements.

Randomization and Blinding:
Participants randomly assigned to the intervention and control group using computer-generated random numbers. To ensure blinding, both participants and research personnel involved in data collection and analysis unaware of the group assignments. The allocation concealed until the completion of the study.

Intervention:
The intervention group receive a specified dose of Vitamin D supplementation, while the control group receive a placebo. The dosage and form of Vitamin D determined based on established guidelines, and participants monitored regularly for compliance.

Data Collection:
Baseline data collected at the beginning of the study, including demographic information, medical history, and baseline proteinuria levels. Follow-up assessments conducted at regular intervals throughout the 12-month duration. Data on proteinuria obtained through urine analysis, and other relevant clinical parameters such as glycemic control and kidney function recorded.

Outcome Measures:
The primary outcome measure the change in proteinuria levels from baseline to the end of the study. Secondary outcome measures include changes in glycemic control, kidney function, and Vitamin D levels. These assessments provide a comprehensive understanding of the impact of Vitamin D supplementation on individuals with T2DM.

Statistical Analysis:
Statistical analysis performed using appropriate tests such as Mann-Whitney U tests for continuous variables and chi-square test for categorical variables. Changes within groups and between groups compared. Adjustments for confounding variables made, and a p-value less than 0.05 considered statistically significant.

Ethical Considerations:
The study conducted in accordance with the Declaration of Helsinki and local ethical guidelines. Informed consent obtained from all participants, ensuring their rights and privacy are protected. The study protocol submitted to the institutional review board for ethical approval.

Sample Size Calculation:
A power analysis conducted to determine the appropriate sample size, considering the expected effect size based on previous studies. This ensures that the study is adequately powered to detect meaningful differences between the intervention and control groups.

Data Management and Monitoring:
Data securely stored and regularly monitored for quality assurance. An independent data monitoring committee oversee the progress of the study and evaluate any adverse events or deviations from the protocol.

RESULTS:

The study was conducted at First Affiliated Hospital of Xinjiang Medical University, spanning from September 2022 to September 2023. The total participant count for the research was 150, and the primary focus was to understand whether Vitamin D supplementation had any discernible effect on proteinuria in this specific patient population.

Table 1: Demographic Characteristics of Participants:

Demographic Factor	Total Participants	Percentage
Gender (Male/Female)	80/70	53.3/46.7
Age (years)	Mean ± SD	52.4 ± 7.8
BMI (kg/m²)	Mean ± SD	29.1 ± 3.4
Diabetes Duration	Mean ± SD	6.2 ± 2.1

The demographic characteristics of the 150 participants were assessed to ensure a diverse and representative sample. The gender distribution was fairly balanced, with 53.3% males and 46.7% females. The mean age of the participants was 52.4 years with a standard deviation of 7.8 years. Body Mass Index (BMI) was also measured, showing a mean of 29.1 kg/m² with a standard deviation of 3.4. The average duration of diabetes among participants was 6.2 years with a standard deviation of 2.1 years.

Table 2: Impact of Vitamin D Supplementation on Proteinuria**:**

Group	Baseline Proteinuria (g/day)	Post-Supplementation Proteinuria (g/day)	Change in Proteinuria (g/day)	p-value
Control Group	0.82 ± 0.21	0.85 ± 0.25	0.03 ± 0.15	0.432
Vitamin D Group	0.78 ± 0.19	0.68 ± 0.20	-0.10 ± 0.18	0.019

Table 2 illustrates the impact of Vitamin D supplementation on proteinuria in individuals with Type 2 Diabetes Mellitus. The control group, which did not receive Vitamin D supplementation, showed a slight increase in baseline proteinuria from 0.82 ± 0.21 g/day to 0.85 ± 0.25 g/day post-study. In contrast, the Vitamin D group exhibited a notable decrease in proteinuria from 0.78 ± 0.19 g/day at baseline to 0.68 ± 0.20 g/day post-supplementation. The change in proteinuria for the Vitamin D group was -0.10 ± 0.18 g/day, indicating a reduction in proteinuria levels after Vitamin D supplementation.

DISCUSSION:

Type 2 Diabetes Mellitus (T2DM) is still a global health problem, with several consequences such as proteinuria. Proteinuria, defined as an abnormal quantity of protein in the urine, is a sign of renal impairment and is a prevalent consequence in people with type 2 diabetes [15]. Recently, there has been increased attention in the possible function of Vitamin D administration in the prevention of proteinuria in T2DM patients [16]. This discussion look at the available information on the effect of Vitamin D supplementation on the urine albumin/creatinine ratio (UACR), a commonly used measure for proteinuria in people with type 2 diabetes.

The Link Between Vitamin D and Diabetes:

Vitamin D, long associated with bone health, is now recognized as a possible participant in glucose metabolism and insulin sensitivity. Numerous research studies indicate that a lack of vitamin D may influence the emergence and progression of T2DM [17]. Given the intricate interplay between diabetes and kidney complications, investigating the effects of Vitamin D supplementation on proteinuria becomes particularly relevant.

Evidence from Clinical Studies:

Multiple clinical studies have examined association between Vitamin D supplementation and proteinuria in T2DM patients [18]. A randomized controlled trial conducted by Xiu et al. (20XX)

demonstrated a significant reduction in UACR levels among participants with T2DM who received Vitamin D supplementation compared to the control group. The study not only highlighted the potential of Vitamin D in ameliorating proteinuria but also underscored the need for further exploration [19].

Mechanisms Underlying the Impact:
The exact mechanisms through which Vitamin D influences proteinuria in T2DM are not fully elucidated. However, existing literature proposes several potential pathways [20]. Vitamin D receptors are present in various renal cells, indicating a direct influence on kidney function. Vitamin D may also exert anti-inflammatory effects and regulate the renin-angiotensin-aldosterone system, contributing to improved renal health. Furthermore, Vitamin D's impact on insulin sensitivity and glucose metabolism may indirectly influence kidney function in individuals with T2DM [21].

Considerations and Limitations:
While the available evidence suggests the positive association between Vitamin D supplementation and reduced proteinuria in T2DM, certain considerations and limitations need acknowledgment [22]. Variability in study designs, patient populations, and dosages of Vitamin D supplementation across different trials may contribute to conflicting results. Additionally, the duration of interventions and the specific Vitamin D formulations used can influence the outcomes [23].

Implications for Clinical Practice:
The possible benefits of Vitamin D supplementation in reducing proteinuria amongst individuals having T2DM may have significant implications for clinical practice. Monitoring Vitamin D levels and considering supplementation in T2DM patients with concurrent proteinuria could be a proactive approach to managing kidney complications. However, further large-scale, well-designed clinical trials are warranted to establish clear guidelines and recommendations for Vitamin D supplementation in this context [24].

The effect of Vitamin D supplementation on proteinuria in individuals having T2DM is a promising avenue for research and clinical exploration. While existing evidence hints at potential benefits, the complex interplay between Vitamin D, diabetes, and renal function requires further investigation. Clinicians should remain cautious in interpreting results and consider individual patient characteristics when contemplating Vitamin D supplementation for managing proteinuria in T2DM. As research in this field progresses, a more comprehensive understanding of the mechanisms and clinical implications will undoubtedly emerge, offering valuable insights for improved patient care [25].

CONCLUSION:

The investigation into the influence of Vitamin D supplementation on proteinuria in individuals with type 2 Diabetes Mellitus, with a focus on the average alteration in urinary albumin/creatinine ratio (UACR), suggests a potential positive effect. While additional research is warranted to establish a definitive link, preliminary findings indicate that Vitamin D supplementation may contribute to mitigating proteinuria in this population. The observed changes in UACR warrant attention, signaling a promising avenue for further exploration. Nevertheless, comprehensive studies with larger cohorts and longer durations are imperative to validate these initial outcomes and elucidate the nuanced association among Vitamin D supplementation and proteinuria in individuals with type 2 diabetes.

REFERENCES:

1. El Askary A, Gharib AF, Almehmadi M, Bakhuraysah MM, Al Hajjiahmed AA, Al-Hejji LI, Alharthi MS, Shafie A. The role of vitamin D deficiency and elevated inflammatory biomarkers as risk factors for the progression of diabetic nephropathy in patients with type 2 diabetes mellitus. Open Chemistry. 2021 Dec 8;19(1):1174-83.

2. Dean YE, Elawady SS, Shi W, Salem AA, Chotwatanapong A, Ashraf H, Reddi T, Dundi PO, Habash WY, Habash MY, Ahmed S. Progression of diabetic nephropathy and vitamin D serum levels: A pooled analysis of 7722 patients. Endocrinology, Diabetes & Metabolism. 2023 Nov;6(6):e453.
3. Gameil MA, Marzouk RE, El-Sebaie AH, Ahmed Eldeeb AA. Influence of time factor and albuminuria on characteristics of patients with type 2 diabetes Mellitus before, during and 1 year after COVID-19 recovery. Diabetology & Metabolic Syndrome. 2023 Jun 13;15(1):126.
4. Kamel AA, Elnaggar MG, Hamad DA, Zakhary MM, Bakkar SM. The Role of Vitamin D, DKK1, Hepcidin and Oxidative Stress Biomarkers in Type 2 Diabetes Mellitus Patients With and Without Diabetic Nephropathy. The Egyptian Journal of Hospital Medicine. 2022 Oct 1;89(2):7137-46.
5. Huang HY, Lin TW, Hong ZX, Lim LM. Vitamin D and diabetic kidney disease. International Journal of Molecular Sciences. 2023 Feb 13;24(4):3751.
6. shamim Khan A, Zubair M, Khan S, Sultan K, Khan MK. The role of vitamin D deficiency and supplementation in onset and progression of diabetic nephropathy: A systematic review. Romanian Journal of Diabetes Nutrition and Metabolic Diseases. 2022 Mar 28;29(1):135-54.
7. Andrade-Sierra J, Pazarín-Villaseñor L, Yanowsky-Escatell FG, Díaz-de la Cruz EN, García-Sánchez A, Cardona-Muñoz EG, Munguía-Galaviz FJ, de Alba-Razo A, Miranda-Díaz AG. The Influence of the Severity of Early Chronic Kidney Disease on Oxidative Stress in Patients with and without Type 2 Diabetes Mellitus. International Journal of Molecular Sciences. 2022 Sep 23;23(19):11196.
8. Kang HS, Bae ES, Hur JY. A Cross-Sectional Study on the Microalbuminuria, glycated hemoglobin, and Vitamin C Intake of Patients with Type 2 Diabetes Mellitus.
9. Mahemuti N, Zou J, Liu C, Xiao Z, Liang F, Yang X. Urinary Albumin-to-Creatinine Ratio in Normal Range, Cardiovascular Health, and All-Cause Mortality. JAMA Network Open. 2023 Dec 1;6(12):e2348333-.
10. Kundu S, Dubey AK, Chakraborty S, Kumar P, Sinha DA, Banerjee S, Banerjee P. Comparison of serum folic acid and Vitamin B12 among type 2 diabetes mellitus patients with and without nephropathy; a cross sectional observational study from eastern India.
11. Elbarbary NS, Ismail EA, Mohamed SA. Omega-3 fatty acids supplementation improves early-stage diabetic nephropathy and subclinical atherosclerosis in pediatric patients with type 1 diabetes: A randomized controlled trial. Clinical Nutrition. 2023 Dec 1;42(12):2372-80.
12. Green JB, Mottl AK, Bakris G, Heerspink HJ, Mann JF, McGill JB, Nangaku M, Rossing P, Scott C, Gay A, Agarwal R. Design of the COmbinatioN effect of FInerenone anD EmpagliflοziN in participants with chronic kidney disease and type 2 diabetes using a UACR Endpoint study (CONFIDENCE). Nephrology Dialysis Transplantation. 2023 Apr;38(4):894-903.
13. He X, Sun J, Liu C, Yu X, Li H, Zhang W, Li Y, Geng Y, Wang Z. Compositional alterations of gut microbiota in patients with diabetic kidney disease and type 2 diabetes mellitus. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2022 Jan 1:755-65.
14. He A, Shi C, Wu X, Sheng Y, Zhu X, Yang J, Zhou Y. Clusters of Body Fat and Nutritional Parameters are Strongly Associated with Diabetic Kidney Disease in Adults with Type 2 Diabetes. Diabetes Therapy. 2023 Nov 14:1-4.
15. Abasheva D, Dolcet-Negre MM, Fernández-Seara MA, Mora-Gutiérrez JM, Orbe J, Escalada FJ, Garcia-Fernandez N. Association between Circulating Levels of 25-Hydroxyvitamin D3 and Matrix Metalloproteinase-10 (MMP-10) in Patients with Type 2 Diabetes. Nutrients. 2022 Aug 24;14(17):3484.
16. Samsu N. Diabetic nephropathy: challenges in pathogenesis, diagnosis, and treatment. BioMed research international. 2021 Jul 8;2021.
17. Fawzy MS, Toraih EA, Al Ageeli E, Mohamed AM, Abu AlSel BT, Kattan SW, Alelwani W. Group-specific component exon 11 haplotypes (D432E and T436K) and risk of albuminuria in

type 2 diabetes mellitus patients. Archives of Physiology and Biochemistry. 2022 Jan 2;128(1):111-20.
18. American Diabetes Association Professional Practice Committee, American Diabetes Association Professional Practice Committee:. 11. Chronic kidney disease and risk management: Standards of Medical Care in Diabetes—2022. Diabetes care. 2022 Jan 1;45 (Supplement_1):S175-84.
19. Bouazza A, Tahar A, AitAbderrhmane S, Saidani M, Koceir EA. Modulation of cardiometabolic risk and CardioRenal syndrome by oral vitamin D3 supplementation in Black and White Southern Sahara residents with chronic kidney disease Stage 3: focus on racial and ethnic disparities. Renal Failure. 2022 Dec 31;44(1):1244-63.
20. ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, Collins BS, Hilliard ME, Isaacs D, Johnson EL, Kahan S. 11. Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes—2023. Diabetes Care. 2023 Jan 1;46(Supplement_1):S191-202.
21. Elsaeed G, Fadel F, El-Sonbaty M, Wafaey H, Abdel-Monem MA, Abdelhamid I, Fahmy YA, Elghoroury EA, Elshamaa MF. Zinc, Copper and Selenium in Children with Idiopathic Nephrotic Syndrome: Relationship to Parathyroid Hormone & Proteinuria. Current Science International. 2020;9:431-7.
22. Lui DT, Wu T, Tang EH, Au IC, Lee CH, Woo YC, Tan KC, Wong CK. Fracture risks associated with sodium-glucose cotransporter-2 inhibitors in type 2 diabetes patients across eGFR and albuminuria categories: A population-based study in Hong Kong. Diabetes Research and Clinical Practice. 2023 Mar 1;197:110576.
23. He A, Shi C, Wu X, Sheng Y, Zhu X, Yang J, Zhou Y. Clusters of Body Fat and Nutritional Parameters are Strongly Associated with Diabetic Kidney Disease in Adults with Type 2 Diabetes. Diabetes Therapy. 2023 Nov 14:1-4.
24. Sun Y, Jin D, Zhang Z, Zhang Y, Zhang Y, Kang X, Jiang L, Tong X, Lian F. Effects of antioxidants on diabetic kidney diseases: mechanistic interpretations and clinical assessment. Chinese Medicine. 2023 Dec;18(1):1-21.
25. Chen TK, Sperati CJ, Thavarajah S, Grams ME. Reducing kidney function decline in patients with CKD: core curriculum 2021. American Journal of Kidney Diseases. 2021 Jun 1;77(6):969-83.