

## ASSOCIATION OF DIETARY PATTERNS WITH SOME RISK BIOMARKERS OF CHRONIC KIDNEY DISEASE OF SAUDI PATIENTS

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### Abstract: -

Chronic kidney disease (CKD) is a worldwide public health problem. There has been a marked rise in the prevalence of (CKD) in Saudi Arabia. This study aimed to identify dietary pattern of Saudi CKD patients and to evaluate the relationship between dietary patterns and the biomarkers in CKD. The study was conducted among 58 previously diagnosed with CKD, both genders, aged > 70 years. Information regarding dietary patterns, demographic and medical history variables was obtained with an online questionnaire. Four dietary patterns, were identified, explaining 54.06% of the variance; Veggie Dietary Pattern, Plant-based Dietary Pattern, Miscellanies Pattern, and Animal-based Dietary Pattern. Correlation between dietary patterns and the metabolic risk factors of CKD; glomerular filtration rate (G3a, G3b), Serum creatinine, and albumin/creatinine ratio, showed inverse significant association with Veggie Dietary Pattern and the metabolic risk factors ( $r -0.591 P .008$ ,  $r -0.574 P.015$ ,  $r -.607 P.007$ ,  $r -.601P.007$ ) respectively. while Animal-based Dietary Pattern was most closely associated with metabolic risk factors ( $r.557 P.021$ ,  $r.551 P.023$ ,  $r.661, P.001$ ,  $r.660 P.001$ ) respectively. Marginally significant association was found between Plant-based Dietary Pattern and Miscellanies Pattern with CKD complications.

After adjustment for age, gender, and BMI same correlation still found.

**Key words:** Dietary pattern. Chronic kidney disease. glomerular filtration rate. Serum creatinine. albumin/creatinine ratio



## 1. INTRODUCTION

Chronic kidney disease has a high global prevalence between 11 to 13% with the majority stage 3 (1). CKD can lead to conditions such as cardiovascular diseases and endstage renal disease (2). There has been a marked rise in the prevalence and incidence of (CKD) in Saudi Arabia due to massive urbanization that has occurred over the last 2 decades (3). Proper dietary management may help to slow the progression of kidney disease. Studies showed that food patterns may have stronger effects on health than any single component (4).

This study was designed to assess the dietary patterns and their associations with biomarkers of patients with (CKD) at the pre-dialysis stage.

## 2. Materials and Methods

### 2.1. Participants:

The study recruited outpatients who consecutively attended hospitals in Makkha area. For participation in the study, the inclusion criteria specified were; diagnosis of chronic kidney disease (CKD) with glomerular filtration rate (GFR) of Stage 3 (G3a, G3b mL/min per 1.73 m<sup>2</sup>), both genders, less than 70 years, and desired to participate freely in the study. The exclusion criteria were; pregnancy, end-stage renal or liver disease, , and failing to complete the online questionnaire. A total of 58 sample completed an online questionnaire reporting their demographic, anthropometric, biochemical features, and dietary patterns.

### 2.2. Demographic features:

Include information about sex, age, smoking, amount of meals /day.

### 2.3. Anthropometric and biochemical Evaluation:

Patients were asked to record information about: anthropometric data (weight, height); marker of CKD biochemical data [glomerular filtration rate (GFR), serum creatinine, albumin-to-creatinine ratio (ACR)]; and clinical data (comorbidities associated with CKD hypertension, diabetes, cardiovascular diseases) from hospital patient's recent medical records.

### 2.4. Dietary patterns:

Online food-frequency questionnaire (FFQ) with 78-food items was administered to appraise the usual food intake. The FFQ was a modified version of the NHANES Food Frequency Questionnaire (FFQ) (5). The food frequency questionnaire was validated for the Saudi population. Participants were asked to indicate how often, on average, they had consumed a given amount of the specified food. Each such item provided nine possible responses, ranging from "never or less than once a month" to "6 -7 times per day".

### 2.5. Statistical analysis:

2.5.1. Anthropometric and biochemical variable: continuous variables are presented as means  $\pm$  SD. Categorical variables are presented as frequencies..

2.5.2. Dietary patterns: were obtained by exploratory factor analysis of the eight food groups. An orthogonal rotation procedure was used which results in uncorrelated factors. Number of extracted factors was first based on the Kaiser criterion, namely eigenvalues  $>1.0$ . In interpreting the rotated factor pattern, a selected food was considered to load on a given factor if the factor loading was  $\geq 0.30$  for that factor and  $<0.30$  for all other factors. No food item was permitted to load more than one factor. The observed Kaiser-Meyer-Olkin (KMO) was 0.786 and Bartlett Test of Sphericity (BTS) is significant  $<.001$ , which meant that the sample was considered to be adequate for factor analysis.

The correlation between dietary patterns factors and the metabolic risk factors of CKD were tested with linear regression model. The predictive accuracy of linear regression model is measured by R. In multivariate models, trend for BMI, gender and age across each dietary pattern were adjusted. The selection of confounders was based on prior consideration of their associations with risk of CKD.

## 3. Results:

### 3.1. Demographic, Clinical and Anthropometric Findings:

Table (1) presents Characteristics of the study subjects

**Table1: Characteristics of study subjects**

| Parameter                               | Variable                          | Response         |
|-----------------------------------------|-----------------------------------|------------------|
| Gender %                                | Male                              | 34(58.62%)       |
|                                         | Female                            | 24 (41.38%)      |
| Age/ years<br>Mean                      | Male                              | (57. 20 ± 9. 45) |
|                                         | Female                            | (54. 16 ± 10.42) |
|                                         | All                               | (55.62 ± 9.73)   |
| Body Mass Index (BMI) kg m <sup>2</sup> | < 18.5                            | 28(48.28%)       |
|                                         | 18.5 – 25                         | 27(46.55%)       |
|                                         | >25- <30                          | 3(5.17%)         |
|                                         | Mean (< 18.5 - <30 )              | 22.32±10.70      |
| Smoking                                 | Yes                               | 17 (29.31%)      |
|                                         | No                                | 41 (70.69%)      |
| number of meals /day                    | Once/day                          | (0.00%)          |
|                                         | 2-3 meals/day                     | 23 (29.31%)      |
|                                         | 4-5 meals/day                     | 34 (29.31%)      |
|                                         | 6-7 meals/day                     | 1 (29.31%)       |
| Co-morbidities                          | Hypertension                      | 21 (36.21%)      |
|                                         | Diabetes                          | 16 (27.59%)      |
|                                         | Cardiovascular diseases           | 13 (22.41%)      |
|                                         | Diabetes &Cardiovascular diseases | 8 (13.79%)       |

**3.2. Biochemical Parameters of CKD Findings:**

Table (2) presents biochemical parameters of CKD of the study subjects

**Table 2: Biochemical Parameters of CKD Participants**

| Parameter                                                       | Sex    | mean         | No |
|-----------------------------------------------------------------|--------|--------------|----|
| glomerular filtration rate (GFR):<br>mL/min/1,73 m <sup>2</sup> | G3a    | 51.5 ± 12.71 | 37 |
|                                                                 | G3b    | 34.2 ± 19.31 | 21 |
| Serum creatinine: mg/dL                                         | All    | 2.45 ± mg/dL | 58 |
|                                                                 | male   | 2.89 ±mg/dL  | 34 |
|                                                                 | female | 1.97 ± mg/dL | 24 |
| albumin/creatinine<br>(ACR):mg/g ratio                          | All    | 75.21± mg/g  | 58 |
|                                                                 | male   | 75.6 ± mg/g  | 34 |
|                                                                 | female | 74.5 ± mg/g  | 24 |

**3.3. Dietary Components:**

Four components were extracted through factor analysis, based on the Kaiser criterion and the scree plot (Figure 1). These four components accounted for 54.06% of the variability within the sample. The factor loading matrix for the major dietary patterns identified among sample surveyed are shown in (Table3). The first pattern, which accounted for 24.01% of the total variance, had high loadings on cucumber, zucchini, , carrots, apple, pineapple green beans, pepper (green), cauliflower, purslane, parsley, broccoli, peas, pear, red grape cabbage, pumpkin radishes, onion. Since this factor was characterized by the intake of vegetables, fruits, it was denoted " Veggie dietary pattern". The second factor explained 15.16% of the total variance. The high-loading foods on the second pattern were loadings on carbohydrates products (Pasta, Breakfast cereal, white rice, white bread, sweet potatoes, brown rice, biscuit; nuts and some legumes: almonds, cashew, pistachios, walnuts, chickpeas, tomatoes) This pattern was denoted " Plant-based dietary pattern". The third factor accounted for approximately 8.28% of the total variance. The high-loading foods on the third pattern were milk and milk products, Chicken without skin, Fish, Olive oil, oil (corn Palm. etc.). This pattern was labeled "Miscellanies pattern". The fourth pattern, denoted the " Animal-based dietary pattern ", was characterized by high loadings with meat and meat products, chickens with skin, egg and lentils. This pattern accounted for approximately 6.61% of the total variance.

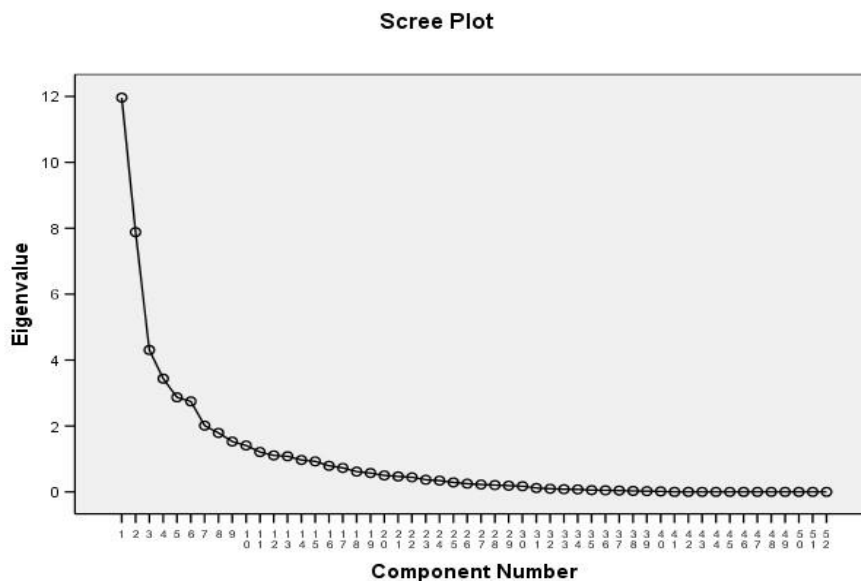


Figure 1: Scree plot of eigenvalue for each component in factor extraction of Food frequency Intake

Table 3: Food Groups with High Factor Loadings for the Four Dietary Patterns

| First component<br>"Veggie dietary pattern" |       | Second component<br>"plant-based dietary pattern" |       | Third component<br>"Miscellanies pattern" |       | Fourth component<br>"Animal-based dietary pattern" |       |
|---------------------------------------------|-------|---------------------------------------------------|-------|-------------------------------------------|-------|----------------------------------------------------|-------|
| cucumber                                    | .951  | Potatoes                                          | .889  | low fat cheese                            | .801  | Lamb                                               | .601  |
| Zucchini                                    | .916  | Pasta (macaroni)                                  | .861  | low fat yogurt                            | .756  | Beef                                               | .548  |
| Carrots                                     | .905  | Breakfast cereal                                  | .857  | Low fat milk                              | .732  | Meat organ                                         | .494  |
| Apple                                       | .903  | Rice( white)                                      | .802  | Labnah                                    | .709  | Processed meat                                     | .437  |
| Pineapple                                   | .845  | White bread                                       | .787  | low fat cheese                            | .648  | Chicken with skin                                  | .356  |
| pear                                        | .826  | Sweet Potatoes                                    | .770  | Chicken without skin                      | .595  | egg                                                | .411  |
| Green beans                                 | .816  | Rice(brown)                                       | .679  | Fish (sea products)                       | .560  | Lentils                                            | .342  |
| Pepper (green)                              | .781  | Biscuit                                           | .666  | Olive oil                                 | .482  | Beans                                              | .311  |
| cauliflower                                 | .751  | Brown bread                                       | .582  | oil (corn Palm.. etc.                     | .461  |                                                    |       |
| Purslane                                    | .666  | Chickpeas                                         | .545  | whole fat cheese                          | .431  |                                                    |       |
| Parsley                                     | .651  | Almonds                                           | .524  |                                           |       |                                                    |       |
| Broccoli                                    | .650  | Cashew                                            | .501  |                                           |       |                                                    |       |
| peas                                        | .543  | Pistachios                                        | .499  |                                           |       |                                                    |       |
| Red grapes                                  | .506  | Walnuts                                           | .441  |                                           |       |                                                    |       |
| pumpkin                                     | .502  | Cake                                              | .387  |                                           |       |                                                    |       |
| Cabbage                                     | .501  |                                                   |       |                                           |       |                                                    |       |
| radishes                                    | .498  |                                                   |       |                                           |       |                                                    |       |
| Onions                                      | .435  |                                                   |       |                                           |       |                                                    |       |
| Initial Eigenvalues                         | 11.91 |                                                   | 7.88  |                                           | 4.31  |                                                    | 3.44  |
| % of Variance                               | 24.01 |                                                   | 15.16 |                                           | 8.28  |                                                    | 6.61  |
| Cumulative %                                | 24.01 |                                                   | 39.17 |                                           | 47.45 |                                                    | 54.06 |
| Frequency of factor%                        | 34.61 |                                                   | 28.85 |                                           | 21.16 |                                                    | 15.38 |

Extraction Method: Principal Component Analysis.  
Rotation Method: Promax with Kaiser Normalization.

### 3.4. Associations of Factor Analysis-Derived Pattern Scores with Risk Factors of CKD:

The associations of food pattern with metabolic risk factors of CKD as well as adjusted correlation of dietary patterns with glomerular filtration rate (GFR), serum creatinine, albumin-to-creatinine ratio (ACR) among subjects surveyed are shown in Table (4) and Table (5).

**Table 4: Association between Dietary patterns and Biochemical Factors of CKD among Samples Surveyed**

| Variable                     | glomerular filtration rate |         |        |         | Serum creatinine |         | albumin/creatinine ratio |         |
|------------------------------|----------------------------|---------|--------|---------|------------------|---------|--------------------------|---------|
|                              | G3a                        |         | G3b    |         | r                | P-value | r                        | P-value |
|                              | r                          | P-value | r      | P-value |                  |         |                          |         |
| Veggie dietary pattern       | -0.591                     | .008    | -0.574 | .015    | -.607            | .007    | -0.601                   | .007    |
| Plant-based dietary pattern  | .486                       | .061    | .488   | .060    | .508             | .051    | .509                     | .051    |
| Miscellanies pattern         | -.489                      | .058    | -.481  | .061    | -.524            | .040    | -.528                    | .04     |
| Animal-based dietary pattern | .557                       | .021    | .551   | .023    | .661             | .001    | .660                     | .001    |

Food group analysis showed that "Veggie dietary pattern" was inversely correlated with the metabolic risk factors of CKD ( $p$  values range .007 - .031). Adjustment for BMI, gender and age did not substantially change the associations. Analysis showed that "Animal-based dietary pattern" was positively correlated with the metabolic risk factors of CKD ( $p$  values range .001 - .023). Adjustment for BMI, gender and age did not substantially change the associations. Thus, "Animal-based dietary pattern" remains independent predictor of CKD risk factors. The "plant-based dietary pattern" was no longer associated with glomerular filtration rate, but positively correlated with serum creatinine and albumin/creatinine ratio, however, marginally insignificant. The "Miscellanies pattern" was no longer associated with glomerular filtration rate, but inversely correlated with serum creatinine and albumin/creatinine ratio. The "Plant-based dietary pattern" and "Miscellanies pattern" were no longer associated with the metabolic risk factors of CKD after adjustment for BMI, gender and age.

**Table 5: Multivariate adjusted Correlation of Dietary patterns with Biochemical Factors of CKD among Samples Surveyed**

| Variable                            | Glomerular filtration rate |         |       |         | Serum creatinine |         | Albumin/creatinine ratio |         |
|-------------------------------------|----------------------------|---------|-------|---------|------------------|---------|--------------------------|---------|
|                                     | G3a                        |         | G3b   |         | r                | P-value | r                        | P-value |
|                                     | r                          | P-value | r     | P-value |                  |         |                          |         |
| <b>Veggie dietary pattern</b>       |                            |         |       |         |                  |         |                          |         |
| Model 1 (unadjusted)                | -.591                      | .008    | -.574 | .015    | -.607            | .007    | -.601                    | .007    |
| Model 2†                            | -.590                      | .008    | -.570 | .015    | -.606            | .007    | -.598                    | .008    |
| Model 3‡                            | -.566                      | .020    | -.551 | .023    | -.601            | .007    | -.598                    | .008    |
| Model4‡                             | -.548                      | .023    | -.541 | .031    | -.596            | .008    | -.581                    | .010    |
| <b>Plant-based dietary pattern</b>  |                            |         |       |         |                  |         |                          |         |
| Model 1 (unadjusted)                | .486                       | .061    | .488  | .060    | .508             | .051    | .509                     | .051    |
| Model 2†                            | .480                       | .062    | .481  | .062    | .498             | .057    | .491                     | .057    |
| Model 3‡                            | .479                       | .062    | .484  | .060    | .490             | .057    | .481                     | .062    |
| Model4‡                             | .474                       | .063    | .473  | .063    | .483             | .060    | .480                     | .061    |
| <b>Miscellanies pattern</b>         |                            |         |       |         |                  |         |                          |         |
| Model 1 (unadjusted)                | -.489                      | .058    | -.481 | .061    | -.524            | .040    | -.528                    | .04     |
| Model 2†                            | -.474                      | .063    | -.479 | .061    | -.503            | .056    | -.504                    | .056    |
| Model 3‡                            | -.472                      | .063    | -.477 | .061    | -.503            | .056    | -.503                    | .056    |
| Model4‡                             | -.469                      | .064    | -.468 | .062    | -.501            | .056    | -.505                    | .054    |
| <b>Animal-based dietary pattern</b> |                            |         |       |         |                  |         |                          |         |
| Model 1 (unadjusted)                | .557                       | .021    | .551  | .023    | .661             | .001    | .660                     | .001    |
| Model 2†                            | .554                       | .022    | .552  | .023    | .655             | .002    | .646                     | .005    |
| Model 3‡                            | .554                       | .022    | .550  | .023    | .638             | .006    | .640                     | .006    |
| Model4‡                             | .550                       | .023    | .550  | .023    | .631             | .006    | .630                     | .006    |

† Adjusted by BMI  
 ‡ Adjusted by gender  
 ‡ Adjusted by age (years),

#### 4. Discussion:

CKD is defined as abnormalities of kidney structure or function, with health consequences. Saudi population is experiencing changes in their dietary habits in the last two decades with accompanying increase in chronic diseases rate including CKD. Dietary modifications may play an important role in the etiology and progression of CKD. The main objective of this study is to identify dietary pattern in chronic kidney disease of Saudi out patients' participants and to determine the correlation between dietary patterns identified and metabolic risk factors i.e. GFR, serum creatinine and albumin/creatinine ratio.

Four dietary patterns: "Veggie dietary pattern", "Plant-based dietary pattern", "Miscellanies pattern" and "Animal-based dietary pattern" were identified (Table 3). Subjects who followed the "Animal-based dietary pattern" were found to have a risk of biomarkers of CKD. In contrast, the "Veggie dietary pattern" was inversely associated with risks of CKD. Meanwhile, both the "plant-based dietary pattern" and "Miscellanies pattern" were marginally either positively or inversely associated with metabolic risk factors of CKD.

Veggie dietary pattern of this study was characterized by higher consumption of vegetables and fruits. Previous research suggests that increased vegetable intake could lead to a decrease in risk of CKD and mortality (6). In the Multiethnic Study of Atherosclerosis, dietary patterns characterized by consumption of fruits and vegetables were associated with lower albumin/creatinine ratio (7). Purslane was One of component of the "Veggie dietary pattern" of the present study. Results of Ghara and Ghadi (8) study showed that purslane administration decreased the elevated level of creatinine and BUN in rats. This study revealed that purslane improved some kidney function parameters due to its antioxidant and antiinflammatory properties.

Chauveau and Lasseur (9). stated that higher consumption of fruits and vegetables is associated with less inflammation and oxidative stress. Nettleton et.al. (7). reported that diets high in whole grains, fruits or vegetables, and fish are inversely associated with markers of inflammation including C-reactive protein (CRP) whereas a diet pattern high in fats and processed meats was directly associated with markers of inflammation including CRP. Kshirsagar et.al. (10) indicated that inflammation might be one possible pathophysiologic link between dietary patterns and microalbuminuria. A large, nationally representative data set showed association of serum C-reactive protein (CRP), with microalbuminuria, a marker of early kidney injury and concluding that elevated levels of serum C-reactive protein (CRP), may play a role in kidney disease. Elevated CRP levels are associated with micro/macroalbuminuria independent of diabetes, hypertension and other potential confounders. This suggests that inflammation may play a role in early kidney damage (11). Animal-based dietary pattern identified by the present study was characterized with meat and meat products, chickens with skin, egg and lentils. The positive association with meat consumption with CKD's risk factors in this study (Table 4) is consistent with similar patterns in several other studies. Bernstein et.al. (12). stated that animal protein causes dynamic effects on renal function. The finding of a study of Nettleton et.al. (7) showed that a dietary pattern with lower red meat and carbohydrates content was associated with lower risks of kidney failure. In a Cochrane review of low protein diets among people with CKD, a delay in progression of CKD was observed with a low protein intake (13). A dietary pattern consisting mostly of processed and fried foods, organ meats, and sweets has been found to be associated with an increased risk of mortality in patients with CKD (14). Lew et.al. (15) stated that red meat intake strongly associated with ESRD risk. Study of Harig, et al. (16) found that there was varied associations of specific dietary protein sources with risk of incident CKD with red and processed meat being adversely associated with CKD risk.

Metabolic studies tend to suggest positive associations between higher consumption of acid foods and risk of CKD. Published data have shown that red meat generally yields greater acid production than other animal-sourced protein (17). Lower daily acid load is associated with better control of acidosis. Dietary acid is thought to promote the progression of CKD; a higher dietary acid load can cause metabolic acidosis and lead to increased risk for kidney disease progression (18). Thus, a dietary balance between acid-producing (e.g., animal sources of protein) and base-producing (e.g., vegetables and fruit) foods is important. High dietary acid load has been shown to be associated with higher incidence of ESRD in the general population in the United States (17). Conversely, plant-based proteins (e.g., soy and legumes) and fruits and vegetables have a high basal load (19).

Miscellanies pattern of this study was characterized by higher consumption of low-fat dairy products (Table 3). Previous research suggests that dairy products may decrease the risk of CKD. Results of study carried by Bernstein et.al. (12) showed that intakes of dairy products, particularly low-fat dairy, had an inverse association with CKD. In Study of Atherosclerosis, dietary patterns characterized by consumption of low-fat dairy were associated with lower albumin/creatinine ratio (7). Study of Lew et.al. (15) showed that intake of poultry, fish, eggs, dairy products did not associate with risk of ESRD. Findings of study of Haring et.al. (16) showed that there was varied associations of specific dietary protein sources with risk of incident CKD; nuts, and low-fat dairy products, and legumes being protective against the development of CKD. Evidence has suggested that protein from dairy may be less detrimental to renal health than protein from nondairy products. These associations were partially explained by dietary components of dairy (monounsaturated fat, polyunsaturated fat, phosphorus, magnesium, calcium, and vitamin D. (20).

Plant-based dietary pattern identified by the present study was characterized by increasing consumption of calorie-dense foods containing whole and refined carbohydrates, and nuts. This study reveals a positive association but insignificant of Plant-based pattern with CKD's risk factors. It is thought that diets high in refined starches, saturated fats, sodium, and lower in whole grains, fruit, vegetables, and fiber may heighten the inflammatory response (21). Elevations in inflammatory markers have been suggested as a biomarker for the incidence of CKD (22). Williams et.al. (23) stated that organizations such as the National Kidney Foundation, the American Kidney Fund, the National Institute of Diabetes and Digestive and Kidney Diseases, and the US Department of Health and Human Services recommend not including whole grains as part of the renal diet. This due to the high phosphorus content in these foods. The positive association, however

insignificant with grains consumption with CKD's risk factors in this study seem inconsistent with similar patterns in several other studies. Dietary patterns characterized by consumption of whole grains, fruits and vegetables were associated with lower albumin/creatinine ratio (7). Bach et.al. (24) stated that a healthy dietary pattern (higher intakes of vegetables, fruit, legumes, nuts, whole grains, fish and low-fat dairy) may prevent CKD and albuminuria.

## 5. Conclusions:

The present study revealed that Animal-based dietary pattern were found to have a risk of biomarkers of CKD. In contrast, the "Veggie dietary pattern" was inversely associated with risks of CKD.

## 6. Recommendations:

Since Saudi people are facing a rapid nutritional and lifestyle transition accompanied by an increase in chronic kidney disease, it appears conceivable that the risk of developing CKD and its complications can be reduced by changing dietary patterns.

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