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# Arabic gum as a natural therapeutic agent for diabetic patients with CKD: A retrospective study

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**ABSTRACT**

Arabic gum (AG) is a dietary additive widely used in food manufacture and drugs; it has also gained popularity as herbal tea that can cure diseases such as diabetes, hypertension, and chronic kidney disease. Studies showed its antioxidant and anti-inflammatory effects. In a retrospective study design, we included CKD patients taking AG for at least three months. Data were collected over one year for each patient: age, co-morbidities, duration, amount of AG used, serum creatinine, inflammatory markers, lipid profile, blood sugar, hemoglobin A1C, and blood pressure readings. For the changes in values and trends, we compared the values individually for each patient separately. A total of 30 patients consisted of 20 males (66.7%) and 10 females (33.3%), with a mean age of 63.2 years. The mean (M) eGFR pre-enrollment in the study was 23.5 ml/min (standard deviation [SD]=15.8), and the mean eGFR at the end of the study was 26.1 ml/min (SD=18.9, p=0.56). There was a significant difference in the eGFR after using AG between diabetics (M=31.3 ml/min, SD=18.5) and non-diabetics (M=20.5 ml/min, SD=18.2, p=0.03). With a history of catheterization, there was a significant difference in eGFR between patients who had catheterization (M=31.76, SD=20.86) and patients without catheterization (M=18.36, SD=13.08, p=0.04). No significant effect on lipid profile, or CRP, yet significant effect on blood sugar control (fasting blood sugar 0.0001, and HBAa1c 0.01). In conclusion, AG is a promising natural material that affects decreasing eGFR in CKD diabetics patients.

**Keywords:** chronic kidney disease, progression, Arabic gum, diabetes

## INTRODUCTION

Arabic gum (AG) or acacia senegal (AS) is a dietary additive that gained popularity because of its diverse use in food manufacturing [1]. It works as a delivery system for many medications used in treating patients and can decrease the toxicity of other medications if used too [2-5]. At the same time, its antioxidant and anti-inflammatory effects made it a hot topic for evaluation in human diseases with background inflammation and activation of inflammatory cascades. AG is used in many diseases like rheumatoid arthritis, gastrointestinal disorders, sickle cell disease, periodontitis, and metabolic disorders for its possible therapeutic effects [6]. chronic kidney disease (CKD) is one of the diseases many researchers showed an early interest in, especially with the use of AG, examining the antioxidant effect on disease progression and outcomes.

Earlier studies on AG were done mainly on rats with Adenine-Induced CKD, which showed the effect of AG on decreasing inflammation and ameliorating oxidative stress. The theory is that AG may reduce adenine-induced inflammation and the generation of free radicals [7-10].

Other effects of AG in rats include the reduction of motor and behavioral changes associated with CKD [11]. In diabetic rats with diabetic nephropathy AG when added to insulin, has its effect on improving glycemic control and stabilization of renal function with a decrease of fibrosis and inflammatory markers like TGFB, endothelin 1 and angiotensin II, which are all implicated in the progression of CKD in these rats [12, 13]. One also cannot forget the effect of AG on the metabolic profile of CKD patients, like decreasing serum urea, creatinine, uric acid, and phosphorus [14].

Our study aims to evaluate the effect of AG on kidney function and metabolic profile of CKD patients visiting the nephrology clinic and taking AG voluntarily as a natural remedy to control their disease as per peer advice from the community. To our knowledge, this is the first study in Jordan and nearby countries to evaluate the effect of AG intake by population to control CKD.

## METHODS

In a retrospective designed study, we included 30 patients with CKD. They were taking AG on their own for at least three consecutive months, between June 2018 till January 2019,

**Table 1.** Baseline characteristics

| Characteristics | Value |
|---|---|
| Age (M±SD) | 63.3 (12.4) |
| eGFR (ml/min [SD]) | 23.5 ml/min (SD=15.8) |
| Gender (n [%]) | |
| Female | 10 (33.3%) |
| Male | 20 (66.7%) |
| Hypertension | 27 (90.0%) |
| Diabetes miletus | 16 (53.3%) |
| Dyslipidemia | 20 (66.7%) |
| Congestive heart failure | 7 (23.3%) |

from nephrology clinics at Jordan University Hospital, a tertiary Jordanian educational hospital.

Our sample was taken from patients regularly following up in the nephrology clinic for CKD care. We included patients who were taking AG voluntarily for at least three months duration. Chronic kidney disease epidemiology collaboration equation (CKD-EPI) equation [15] is usually used in calculating the estimated glomerular filtration rate (eGFR) for these CKD patients in our nephrology clinic.

According to the stage of CKD, our patients were in stages II-V with eGFR between (72.7-5.3) ml/min/$m^2$. We excluded end-stage renal disease patients on regular dialysis and renal transplant patients. Half of the patients are diabetic, and almost all have hypertension (HTN). Combined follow-ups in nephrology and other clinics were noticed. The usual frequency of clinic visits for patients varies between one to three months; we took data related to at least three clinic visits (three-12 months).

Data collected included: age, gender, comorbidities of the patient (having diabetes [DM], HTN, CKD, ischemic heart disease [IHD], dyslipidemia [DL], and recent history of cardiac catheterization during use of AG, duration of AG use, and amount of AG used by patients. Laboratory and clinical data included were lipid profile, serum creatinine, inflammatory markers like erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), hemoglobin A1C (HBA1C), eGFR change and trend, and blood pressure trend during intake of AG.

No change in patients' medications was done during the patients' follow-up unless clinically indicated. For the differences in values and trends, we compared the values individually for each patient separately (reading 1, reading 2, and reading 3).

### Statistical Analysis

Data were entered and analyzed using statistical package for social sciences (SPSS), version 24. $p<0.05$ was assigned as α. Data were assessed for normality using the Shapiro-Wilk test, histograms, and Q-plots. Assumptions for using parametric statistics were satisfactory using Levene's test for equal variances. The effects of sociodemographic variables on serum creatinine, eGFR, blood pressure readings, HBA1c, body mass index (BMI), fasting blood sugar (FBS), duration of AG use, low-density lipoprotein (LDL), high-density lipoprotein (HDL), cholesterol, ESR, and CRP were determined by performing independent samples.

t-test and Mann-Whitney U test for the following factors: the presence of DM, the presence of DM nephropathy, and the presence of catheterization history. A part-test and Wilcoxon sign rank test was used to assess KFT before and after using AG, systolic and diastolic blood pressure reading, creatinine, and GFR trends during the use of AG.

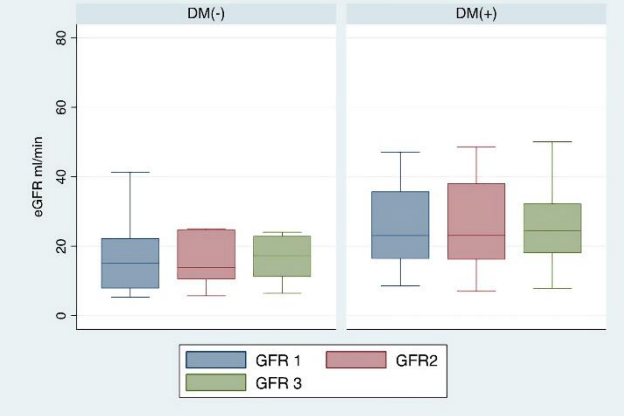


**Figure 1.** eGFR based on DM status (Source: Authors' own elaboration)

## RESULTS

The total of 30 patients consisted of 20 males (66.7%) and 10 females (33.3%), with a mean age of 63.2 years. Descriptive data about the medical history of patients are presented in **Table 1**. The average duration of CKD is 4.5 years, with the average time of AG use 0.8 years.

To show more details in patients with CKD and DM (diabetic nephropathy), There was a significant difference in eGFR after the use of AG between patients with diabetic nephropathy (mean[M]=31.3 ml/min, standard deviation[SD]=18.5) and patients without diabetic nephropathy (M=20.5 ml/min, SD=18.2, p=0.03). **Figure 1** shows the difference in eGFR between diabetics and non-diabetics.

There was a significant difference in eGFR trend during the use of AG (reading 1) between patients with diabetic nephropathy (M=27.8 ml/min, SD=17.2) and patients without diabetic nephropathy (M=18.9 ml/min, SD=14.2, p=0.07). There was a significant difference in eGFR trend during the use of AG (reading 2) between patients with diabetic nephropathy (M=30.01 ml/min, SD=18.4) and patients without diabetic nephropathy (M=21.0 ml/min, SD=19.3, p=0.04). There was a significant difference in eGFR trend during the use of AG (reading 3) between diabetics (M=29.5 ml/min, SD=20.1) and non-diabetics (M=21.1 ml/min, SD=15.8, p=0.08).

Data was not enough to show changes in CRP, and we didn't find any effect on lipid profile [16] in patients while using AG. Still, there was a significant effect on Fasting blood sugar levels and HBA1C, 0.0001 and 0.01, respectively (**Table 2**).

Regarding blood pressure, we did not find any change in blood pressure readings after the use of AG (**Figure 2**). Comparing patients with a history of catheterization, there was a significant difference in eGFR between patients undergoing catheterization during AG use (M=31.76, SD=20.86) and patients without a history of catheterization (M=18.36, SD=13.08, p=0.04) (**Figure 3**).

## DISCUSSION

AG is a polysaccharide that can be found in nature in the form of gummy exudate on the stems and branches of the AS tree. It is edible, and FDA approves it as a food additive widely used in food and drug manufacturing. Studies showed variable

**Table 2.** Effect of arabic gum on laboratory data of DM patients

| Variable | Mean (±SD) | p-value | 95% CI |
|---|---|---|---|
| LDL | 90.6 (54.4) | 0.5000 | -55.10-27.30 |
| HDL | 33.9 (19.1) | 0.3900 | -26.50-10.68 |
| Cholesterol | 145.3 (77.6) | 0.8900 | -56.90-65.20 |
| TG | 149.1 (103.6) | 0.8600 | -82.70-69.10 |
| ESR | 27.4 (33.5) | 0.3000 | -39.60-12.70 |
| CRP | 18.2 (31.5) | 0.7800 | -20.30-26.80 |
| FBS | 201.0 (71.5) | **0.0001** | 59.30-143.30 |
| HbA1C | 7.5 (2.8) | **0.0100** | 0.70-4.10 |
| Uric acid | 7.1 (1.4) | 0.5000 | -0.80-1.60 |

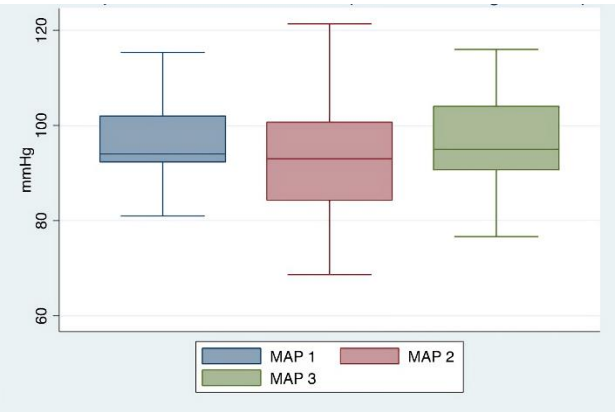


**Figure 2.** Mean arterial blood pressure readings during study follow-up time (Source: Authors' own elaboration)

effects of this material on renal, cardiac, intestinal cells, and metabolism, too [17].

Acting as an antioxidant, anti-inflammatory, and antiapoptotic and decreasing oxidative stress is postulated as the mechanism of action for AG. In addition to its possible effect on monocyte and complement-mediated tissue damage pathways [18, 19], AG will also affect the vascular response in CKD patients, which can contribute to the progression of the disease [20]. Another health benefit of AG can come from its potential prebiotic properties on the gut and decreasing uremic toxins [21-24]. AG can replete the levels of butyrate with its anti-inflammatory, antioxidant capacity, and anti-nitrosative properties that will contribute to the stabilization and treatment of CKD, too [19, 25].

CKD is a global health problem affecting mortality and morbidity. This disease prevalence is between 11 to 13% worldwide, and most cases are in stages 3-4 [26]. The inflammatory background of CKD is implicated in many complications like cardiovascular disease and anemia [27]. At the same time, accumulation of toxins will induce more and more inflammation and increase oxidative stress in body [28].

Many inflammatory markers were studied, like CRP, ESR, cytokines, interleukins, plasma fibrinogen, TNF-a, and serum albumin [29]. The last three were implicated in CKD's progression [27, 30-32]. Many natural materials and remedies are used nowadays by the general population to try to delay the progression of CKD and prevent the unfavorable end of being on dialysis. Researchers studied minerals, vitamins, and plant-derived metabolites that they thought could decrease inflammation and oxidative stress in CKD and delay progression, such as magnesium, selenium, vitamins (A, B1, C, D, and E), flavonoids like quercetin, which can work as an antioxidant, anti-diabetic and anti-inflammatory agent, Curcumin, which can exert antioxidant activity through

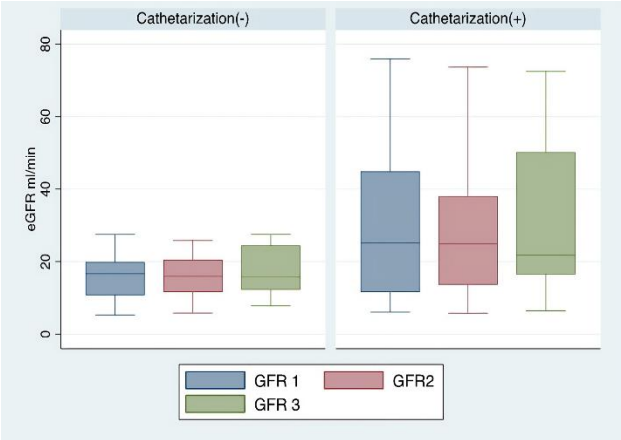


**Figure 3.** eGFR by cardiac catheterization status (Source: Authors' own elaboration)

reacting directly with free radicals and enhance gene expression for protective proteins with antioxidant activity. Resveratrol inhibits lipid peroxidation, chelate ions, and scavenger for free radicals. The list contains many other compounds derived from plants or natural sources [33-35].

During the past few years, with patients being open to various communication and internet recourses, we noticed that many of these patients following for CKD in the nephrology clinic heard about the potential benefit of taking AG and started taking it on their own. Its' availability and relatively low price with trials on a large scale in the community encouraged many of these patients to take it. Crude observation in our nephrology clinic that some patients had changes in creatinine level and eGFR after using AG led us to do this pilot observational study.

Our patients were taking the AG in powder form; the average intake is one-two tablespoons of the material dissolved in water twice daily (14-30 gm per day). All the clinical and laboratory data were gathered during their routine follow-up visit to the clinic according to CKD stage every one-three months. The amount to be used, suggested by different studies on rats and humans is variable [10, 18, 19]. It can be between 10 gm up to 40 gm per day for humans [29].

Being a CKD patient will increase the chance for complications, mainly cardiovascular disease, progression of CKD, with proteinuria on board in these patients [36-41], and DM [42-44], altogether will increase morbidity and mortality [38, 40]. Half of the current cohort underwent percutaneous coronary catheterization for IHD during their intake of AG and follow-up in nephrology clinics.

We compared diabetic patients in our cohort to non-diabetic patients, and we found a significant change in eGFR; we suggest that this could be due to the effect of AG on background inflammation and metabolic profile in diabetics, especially in the presence of CKD [10, 24, 31, 45]. Even though the change in eGFR was borderline statistically significant, it was enough to change the stage of CKD in some patients clinically.

It can also be explained by better blood sugar control (FBS and HBA1C), as suggested by findings in our small number cohort. Studies on rats and humans suggest the effect of AG on blood sugar control and diabetic nephropathy [12, 46]. Another beneficial effect of AG on diabetics, and non-diabetics, could be its effect on decreasing the weight and mass of adipose tissue

[47-50]. Unfortunately, because of the retrospective design and the small number of patients, we could not assess the effect of AG on BMI.

Another important observation in our study was the difference in eGFR between patients who underwent catheterization, which was in favor of patients who received AG, either because of its anti-inflammatory or ant-oxidant effect, which can present in patients with acute coronary syndrome or as a result of contrast media exposure. This can be of great importance, especially with the high association of CKD with cardiovascular risks and diseases [51-53] and may suggest the possible protective vascular effect of AG in patients with CKD [12] and needs catheterization for diagnosis or intervention.

## CONCLUSION

The use of AG in patients with CKD may positively affect decreasing serum creatinine levels and may downgrade the stage of CKD if given to patients with early CKD. This could be due to the anti-oxidative and anti-inflammatory nature of AG, which can affect the background inflammation in CKD, or due to its effect on the metabolic profile of patients. To our knowledge, these issues are not fully answered in humans. This observational study is one of the first to address this idea, even with a small number of patients. We still need more investigations on patients with different CKD stages and further evaluation of the AG on these patients' arterial blood pressure, metabolic profile, and biological and inflammatory markers.

**Author contributions: SAA:** conception, design, literature review, & writing manuscript; **HA:** literature review, data interpretation, & data collection; **OAO:** literature review, analysis & interpretation of data, & writing manuscript; & **KHA:** literature review, interpretation of data, & writing manuscript. All authors have sufficiently contributed to the study and agreed with the results and conclusions.

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**Ethical statement:** Authors stated that the study was approved by the Institutional Review Board of Jordan University Hospital on 08 August 2019 with approval code: 169/2019.

**Declaration of interest:** No conflict of interest is declared by authors.

**Data sharing statement:** Data supporting the findings and conclusions are available upon request from the corresponding author.

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