

# Traditional herbal and non-steroidal anti-inflammatory analgesic (nsaias) usage and its association with chronic kidney disease (CKD) in northern Saudi Arabia

## Abstract

**Background:** The causes of Chronic Kidney Disease (CKD) aren't always known, but most lead to damage of blood vessels in the kidney or other renal structures. Therefore, the aim of this study was to estimate the prevalence of herbal and Non-steroidal Anti-inflammatory Analgesic (NSAIAs), as causes of CKD.

**Methodology:** This study investigated 4240 volunteers, their age ranging from 18 to 90 with a mean age of 42years, of whom 2133 were males and 2107 were females.

**Results:** Traditional herbal preparation usage was indicated in 573/4240(13.5%), OR (95% CI)= 0.521(0.4343-0.625), P<0.0001 and NSAIAs usage was revealed in 456/4240(10.8%), OR (95% CI)= 0.425(0.345-0.522), P<0.0001. Herbal usage was identified among 209/573(36.5%) of the males and 364/573(63.5%) of the females.

**Conclusion:** Considering the growing prevalence of CKD in the Kingdom of Saudi Arabia (KSA) and increasing use of traditional herbal and NSAIAs show the importance of improving our knowledge about different etiological factors. The use of traditional herbal and NSAIAs is relatively prevalent and associated with CKD.

**Keywords:** CKD, herbal, NSAIAs, hypertension, diabetes

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**Abbreviations:** CKD, chronic kidney disease; NSAIAs, non-steroidal anti-inflammatory analgesic; GFR, glomerular filtration rate; NSAID, non-steroidal anti-inflammatory drugs

## Introduction

Chronic Kidney Disease (CKD) is defined as the occurrence of kidney damage or a glomerular filtration rate (GFR)<60ml/min/1.73m<sup>2</sup> for≥3 months.<sup>1</sup> The existence of albuminuria is most ordinarily used to indicate kidney damage, while GFR is usually estimated using equations that comprise a filtration marker, such as serum creatinine.<sup>2</sup> CKD reside clinically silent and therefore undetected until an advanced stage is reached.<sup>3</sup> CKD is a common disorder that regardless of its etiology results in a varied range of comorbidities including hypertension, hyperparathyroidism, anemia, vascular calcification and faster cardiovascular disease.<sup>4</sup> The symptoms related to CKD are unclear and are often attributed to age-linked weakness; as a result CKD often remains undiagnosed until the advanced stage is reached.<sup>5</sup> The global ageing of population and the largely increasing rates of obesity, hypertension, and diabetes propose that the incidence and prevalence of CKD will rise over the subsequent decades.<sup>6,7</sup> Since existing treatment choices for several diseases are limited in many communities, a number of patients seek out alternative treatments such as traditional herbal therapies. However, there is a lack of evidence from large clinical trials to support the safe use of these traditional therapies in many population settings. Several active components of traditional herbal formulas are undetermined and their toxicities are unidentified.<sup>8-10</sup> Nonsteroidal anti-inflammatory drugs (NSAIDs), are broadly used for their anti-inflammatory and analgesic properties.<sup>11</sup> However, long-term utilization of nonselective

NSAIDs could increase the risk of CKD progression. The escaping of NSAIDs in the medium term is unnecessary in patients with moderate to severe CKD, if not then contraindicated. As the meaning of high-dose of NSAID use leftovers unclear, the lowest effective dose of NSAIDs should be prescribed where designated.<sup>12</sup> There has been a noticeable increase in the prevalence and incidence of CKD in KSA over the last three decades. This increase goes beyond those reported from many countries. The massive and fast changes in lifestyle, high population growth, and rapid rise in life expectancy, and great urbanization that has happened over the last three decades combined to make the present CKD status different to what it was. The two major factors that influence the CKD status are the very high rate of diabetic nephropathy and shift in age demographics.<sup>13</sup> However, many risk factors are supposed to contribute to this escalation of CKD in KSA including the use of traditional herbal medications as well as, intensive use of NSAIAs. Therefore, the aim of this study was to assess the prevalence of herbal and NSAIAs usage and its relation with CKD.

## Materials and methods

This study involved a community based cross-sectional survey covered randomly selected 30 primary health centers in Hail region, North KSA. Data regarding herbal usage and NSAIAs were collected from 4240 participants. Data were collected by a professional medical team from College of Medicine, and College of Applied Medical Science, University of Hail. A form was designed to collect the demographic information, such as previously diagnosed DM, age and sex. Information regarding herbal usage and NSAIAs were collected depending on self-reporting. Diagnosis of diabetes in this survey was

based on the information provided by the participant of being under treatment for diabetes due to a previous well-established diagnosis then confirmed with new blood glucose estimation. Diagnosis of hypertension was based on observation of blood pressure levels  $>140/90\text{mmHg}$ . Mean blood pressure was calculated from up to three blood pressure readings taken from participants in a seated position. Hypertension was defined as a mean blood pressure  $\geq140/90$  or current use of medication for hypertension. Blood pressure between  $120/80\text{mmHg}$  and  $139/89\text{mmHg}$  was considered as pre-hypertension. Blood and urine specimens' were collected from each respondent. The results of diagnostic tests performed at that time (urine dipstick, capillary blood glucose) as well as blood pressure levels were also registered in this form.

GFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation.<sup>2</sup> CKD was indicated based on the presence of protein urea and level of GFR. All individuals with a glomerular filtration rate (GFR) $<60\text{mL/min}/1.73\text{m}^2$ , were regarded as having KCD. CKD stages were categorized according to the following:

1. Stage I: Kidney with normal GFR ( $90\text{mL/min}/1.73\text{m}^2$  or above).
2. Stage II: Kidney with mild decrease in GFR (60 to  $89\text{mL/min}/1.73\text{m}^2$ ).
3. Stage III: Kidney with moderate decrease in GFR (30 to  $59\text{mL/min}/1.73\text{m}^2$ ).
4. Stage IV: Kidney with severe reduction in GFR (15 to  $29\text{mL/min}/1.73\text{m}^2$ ).
5. Stage V: Kidney failure (GFR less than  $15\text{mL/min}/1.73\text{m}^2$ ).

### Ethical consent

The protocol of the project was approved by Research Committee, College of Medicine, and University of Hail. Each participant was informed before the interview about the purpose of the survey, and informed consent was obtained from each participant.

### Statistical analysis

Data management was done using Statistical Package for Social Sciences (SPSS version 16). SPSS was used for analysis and to perform Pearson Chi-square test for statistical significance (P value). The 95% confidence level and confidence intervals were used. P value less than 0.05 was considered statistically significant.

## Results

The present study investigated 4240 volunteers, their age ranging from 18 to 90 with a mean age of 42years, of whom 2133 were males and 2107 were females. Traditional herbal preparation usage was indicated in 573/4240(13.5%) and NSAIAAs usage was revealed in 456/4240(10.8%). Herbal usage was identified among 209/573(36.5%) of the males and 364/573(63.5%) of the females. Herbal usage was significantly associated with females, and the odds ratio (OR), its standard error and 95% confidence interval (95% CI) was 0.521(0.4343-0.625), P<0.0001. NSAIAAs usage was identified among 146/456(32%) of the males and 310/456(68%) of the females. usage was significantly associated with females, and OR and 95% CI was 0.425(0.345 -0.522), P<0.0001. The great majority of the herbal users were at age group 41-55years old representing 176/573(30.7%) followed by age groups 26-40 and 56-70 constituting

164/573(28.6%) and 115/573(20%) respectively. For NSAIAAs, most users were found among age group 41-55years followed by age group 26-40 and 56-70years representing 131/456(28.7%), 111/456(24.35) and 110/456(24%), respectively as indicated in Table 1 & Figure 1. Regarding education, most of the herbal users were none educated individuals followed by university level of education. Also most of NSAIAAs users were also none educated followed by primary and university levels, as indicated in Table 1. However, when calculating percentage in each single group, variable proportions can be seen as shown in Figure 2.

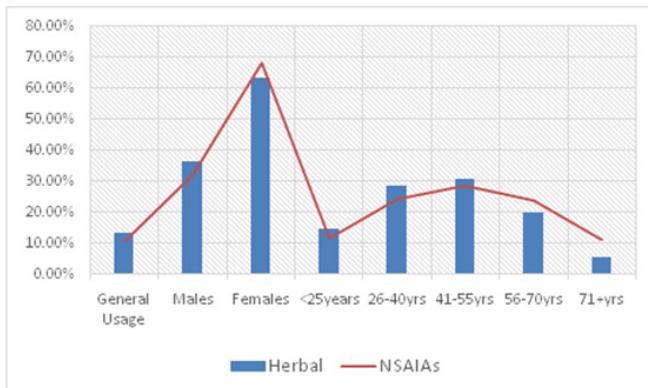


Figure 1 Herbal and NSAIAAs by demographic characteristics.

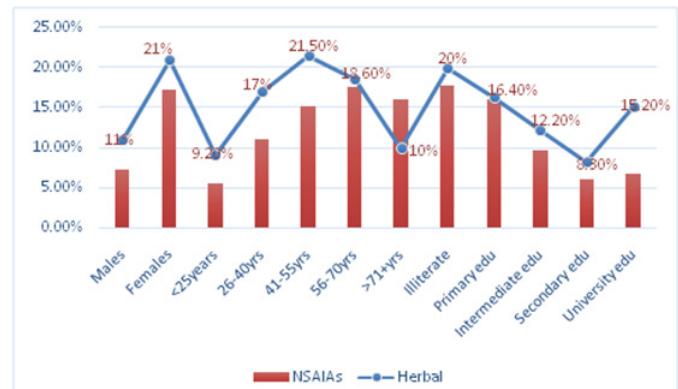


Figure 2 Herbal and NSAIAAs by sex, age and education.

Table 1 Herbal and NSAIAAs by demographic characteristics

Variable	Category	Herbal		NSAIAAs	
		Yes	No	Yes	No
GFR(ml/min/1.73m <sup>2</sup> )	≥90	198	1325	171	1356
	60-89	183	792	170	805
	30-59	37	153	43	147
	15-29	4	11	4	11
	<15	4	7	3	8
Hypertension	Yes	169	925	157	936
	No	401	2728	294	2841
Diabetes	Yes	199	996	161	1035
	No	373	2666	292	2750

Table 2 summarizes the distribution of Herbal and NSAIs usage by CKD, Hypertension and Diabetes. However, about 45/573(7.8%) and 50/456(11%) of the herbal and NSAIs users, respectively were identified with CKD. Of the 45 herbal users with CKD, 37/45(82.2%), 4/45(8.9%) and 4/45(8.9%) were with GFR levels 30-59, 15-29 and <15mL/min/1.73m<sup>2</sup>, respectively. Of the 50 herbal users with CKD, 43/50(86%), 4/50(8%) and 3/50 (6%) were with GFR levels 30-59, 15-29 and <15mL/min/1.73m<sup>2</sup>, respectively. Hypertension and Diabetes were identified in 169/570(%) and 199/572(%) of the herbal users in this order. Hypertension and Diabetes were identified in 157/461(%) and 161/453(%) of the NSAIs users, respectively, as indicated in Figure 3. When comparing the percentages with each variable category, there was a relatively different value as indicated in Figure 4.

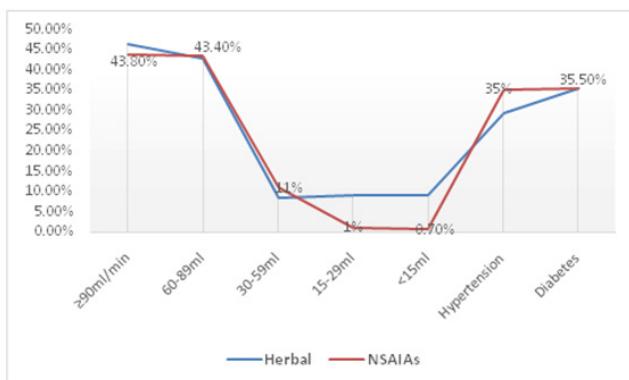


Figure 3 Herbal and NSAIs by GFR levels, hypertension and diabetes.

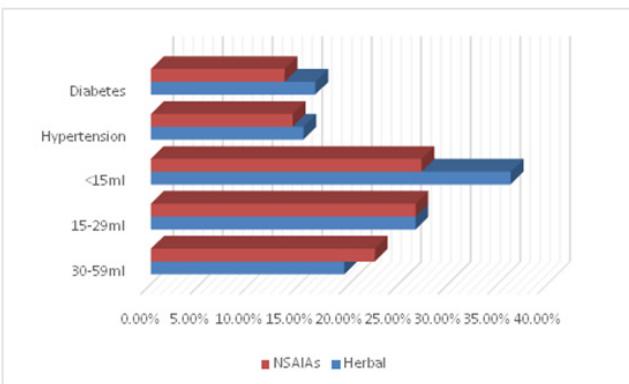


Figure 4 Herbal and NSAIs by CKD, hypertension and diabetes.

Table 2 Herbal and NSAIs by CKD, Hypertension and Diabetes

Variable	Category	Herbal		NSAIs	
		Yes	No	Yes	No
GFR(ml/min/1.73m <sup>2</sup> )	≥90	198	1325	171	1356
	60-89	183	792	170	805
	30-59	37	153	43	147
	15-29	4	11	4	11
	<15	4	7	3	8
Hypertension	Yes	169	925	157	936
	No	401	2728	294	2841
Diabetes	Yes	199	996	161	1035
	No	373	2666	292	2750

## Discussion

The prevalence of CKD is considerably high in general Saudi population, since there is close homology within Saudi population in different regions. The most comprehensive study included a large number of population is from Hail region. The study found a prevalence estimate of 9.4% of CKD.<sup>3</sup> One of the leading issues in CKD prevention is disease awareness towards exposure to different risk factors. Lack of health management, social and traditional believes in non-safe treatment has been shown to have strong impact in the development and progression of CKD, in individuals and in residential populations.<sup>14</sup> Screening and intervention can prevent CKD, and where management strategies have been employed the incidence of CKD has been reduced. Awareness of the disorder, however, remains low in several populations and among many medical doctors. Strategies to reduce burden and costs related to CKD consequence need to be strongly addressed.<sup>15</sup> In the present study the prevalence of herbal use was 13.5% and among females was significantly higher than males. Herbal therapies usage is very public in all most all parts of KSA. Herbal preparations are popular because most of peoples believe that they are natural and safe, more than other synthesized drugs.<sup>16</sup> In KSA, the traditional medicine is mainly built on herbal preparations and spiritual healing, both as a commodity and as homemade mixtures.<sup>17</sup> Although the registration of herbal medications is compulsory in the Saudi Ministry of Health<sup>18</sup> but there are many widely used non-registered herbal preparations. The results of the present study show frequent exposure of community to herbal medications which raised the importance of awareness toward knowledge of any non-registered herbal medications. Suitable educational activities may increase knowledge and awareness regarding herbal preparations, particularly among women. Therefore, there is a need for research to isolate active compounds from traditional herbal medications and know the process of its action, as well as their possible toxicity to kidney, and subsequently implementation if safe. However, well-designed, randomized, controlled, clinical trials are needed to verify the efficacy and safety of their use particularly in patients with CKD.<sup>10</sup> In the current study the prevalence of NSAIs usage was 10.8% among study population and among females (68%) were significantly higher than males (32%). The use of NSAIDs have been linked to acute kidney injury in the general population,<sup>19</sup> as well as with disease progression in those with CKD.<sup>20</sup>

Habitual NSAID abuse can lead to analgesic nephropathy, a disorder that is frequently irreversible upon drug cessation.<sup>21</sup> Though epidemiologic studies have connected NSAID usage to progression of CKD,<sup>22</sup> the risks of NSAIDs in patients with CKD, remain less clearly recognized. The most commonly prescribed drug in KSA was paracetamol followed by ibuprofen, diclofenac, and aspirin. In few of the prescriptions combination of analgesics, antipyretics, and NSAIDs were used. Aspirin was used exclusively in adults for cardio-protection, while paracetamol was used mainly as analgesic-antipyretic.<sup>23</sup> In another recent study 15% of patients received an NSAID treatment: females were more than males. The percentage of patients who received an NSAID prescription across the health centers ranged from 9% to 24%. The main cause for recommending NSAIDs was musculoskeletal problems. The most frequently prescribed NSAID was ibuprofen. Approximately, 6% of patients who received an NSAID drug had a risk factor related to its use. The mean and median duration of the NSAID treatments of all types were 5.6 and 5.0 days, respectively.<sup>24</sup> Even with the potential adverse renal sound effects of NSAIDs, little is well-known about the patterns of NSAID usage amongst those with CKD in community sets.

However in the present study we have just estimated the prevalence and describe self-reported NSAID usage among adults by CKD status using data from the community-based comprehensive survey in Hail region, Northern KSA, which is a limitation in this study. Notably several factors have been identified including hypertension and Diabetes which might be contributed to the burden of CKD in the present study. Also we tried to link factors such as level of education to these means of medication but it seemed that it has no significant effect.

## Conclusion

Considering the growing prevalence of CKD in the Kingdom of Saudi Arabia (KSA) and increasing use of traditional herbal and NSAIDs show the importance of improving our knowledge about different etiological factors. The use of traditional herbal and NSAIDs is relatively prevalent and associated with CKD.

## Conflict of interest

The author declares no conflict of interest.

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