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Comparative Analysis of Effects of Herbal Drugs and Analgesics on Chronic Kidney Disease Pattern in Ha'il, Saudi Arabia

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ABSTRACT

Background: *Chronic kidney disease (CKD) is becoming a major health problem among the elder population in the Hail region, Saudi Arabia. In this present study, our aim was to screen the usage of herbal products in comparison to the non-steroidal anti-inflammatory analgesic (NSAIAs) usage in Hail population (apparently normal) in Saudi Arabia (KSA) and their possible impact on chronic kidney disease (CKD).* ***Methodology:*** *A multi-centre cross-sectional study was carried out with an apparently normal sample population of Hail. The sample was collected from different provinces of Hail region (Al-Zahra, Sidian, Sharaf, Alwesitaa, Lubda, Nasia, Nugra, Samra). The sample was analyzed under group five criteria i.e., based on Hail region, based on gender, based on age, based on creatinine level, and based on the education level, which was evaluated for the screening of drugs usage with reference to chronic kidney disease. The sample population was exposed to two types of drugs, non-steroidal anti-inflammatory drugs (NSAIDs) and herbal products with reference to CKD.* ***Results:*** *The results drawn from the statistical analysis were tabulated. The screening of drugs (analgesics and herbal) on selected groups from a total population of Hail region proved that more herbal products are used than analgesics drugs. Traditional herbal preparation usage was indicated in 216/4565 (12.182%) samples and NSAIAs usage was revealed in 156/4565 (8.798%) samples.* ***Conclusion:*** *The use of traditional herbal therapy and NSAIAs is prevalent in Hail region and it is more apparent among less educated individuals. Traditional herbal therapy proves to be more used than analgesics. The regular use of herbal products and non-steroidal anti-inflammatory drugs (NSAIDs) for a long period may increase the risk of CKD progression.*

Keywords: Analgesics drugs, Herbal drugs, CKD, GFR

INTRODUCTION

Chronic kidney disease (CKD) is mainly caused by diabetes and high blood pressure. It is a slow process of loss of the kidney function over a period of prolonged time, which ultimately leads to the permanent loss [1]. Glomerular filtration rate (GFR) (<60 ml/min/1.73 m^2) for ≥ 3 months causes kidney damage which is often known as chronic kidney disease (CKD) [2]. Early treatment after analysis of CKD is a legitimate enterprise, it gives meaningful opportunities for effective and safe interventions that can reduce the death risk, end-stage renal disease, or complications of renal dysfunction [3]. The etiology of the CKD is not well known, but its impact can be decreased by controlling the blood pressure, glycemic, proteinuria, and smoking cessation. All chronic kidney disease patients are significantly at a high risk of cardio arrest, if we control the function of the kidney it helps to manage the cardiovascular risk factor such as hyperlipidemia [3]. At present, high neutrophil gelatinase-associated lipocalin (NGAL) levels have been detected in patients with heart failure, cardiovascular disease, or stroke [4,5].

The relationship between chronic renal failure (CRF) and many cardiovascular diseases was first detected in the dialysis patients, where cardiovascular disease risk was very high. Approximately 50% of individuals with end-stage renal disease (ESRD) die due to cardiovascular disease or stroke [6,7].

CKD is associated with end-stage renal disease (ESRD) and increases morbidity, mortality, and cost of the healthcare system [8]. The estimated glomerular filtration rate (eGFR) is evaluated on the basis of creatinine-based formulae for the modification of diet in renal disease (MDRD) and chronic kidney disease epidemiology collaboration (CKD-EPI) equations. World Health Organization, United Nations, and the United States, Department of Commerce had shown interest in focusing monitor growth and aging trends worldwide of demographic profiles of Arab countries [8]. In 2014, total average life expectancy was 74.8 years (72.8 years male and 76.9 years female) and predicted to increase. In 2013, the WHO reported that approximately 4.3% of Saudi Arabia population aged between 55 years to 64 years of age, and 2.79% was aged between 65 years of age and above [8].

In 2012, United Nations projected that population of Saudi Arabia between the age group of ≥ 65 will continuously increase, and in 2050, this older population will make to 18.4% of the total population [9]. Increase in the older population prediction will create a direct impact on the healthcare system, care cost and an indirect impact on other services funding of all aspects. On the basis of population, older patients with advanced chronic kidney disease have a tendency to present later for dialysis, which has a higher number of co-morbid conditions, are at a higher risk of cognitive dysfunction and have increased levels of frailty, all combined with potential sensory impairments such as declining vision [10-12]. Unbalance diet uptake is also a major problem for these types of patients. It is difficult for the treatment modality of older patients having these factors with end-stage renal disease (ESRD) [13].

In the multi-center cross-sectional survey 5000 Saudis were selected from 30 primary healthcare centers (PHCs) of Kingdom of Saudi Arabia (KSA) in which the prevalence of 9.4% in CKD was recorded. In general, Saudi population is on the high risk of chronic kidney disease (CKD) due to close homology within Saudi population in different regions [14]. In the Kingdom of Saudi Arabia (KSA) it is reported that many factors are responsible for chronic kidney disease (CKD) including, hypertension, diabetes, obesity and other factors [15-19]. However, there is no noticeable genetic factor instead of diverse causes of chronic kidney disease (CKD) or chronic renal failure (CRF) [20].

The treatment for several diseases are limited, patients seek out alternative treatments such as traditional herbal therapies. But due to lack of evidence from clinical trials traditional therapies are not supported as safe for use in many regions. The toxicities of traditional herbal therapy are unidentified since active components of these herbal drugs are not known [21]. As compared to the traditional herbal therapy non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used for anti-inflammatory and analgesic properties [22]. The regular use of non-steroidal anti-inflammatory drugs (NSAIDs) for a long period increases the risk of CKD progression [23]. The high-dose of NSAIDs are unclear however the lowest effective dose of NSAIDs should be prescribed where designated [24]. In KSA from last three decades, there has been a noticeable increase in the prevalence and incidence [23].

In this present study, our aim was to screen the usage of herbal products in comparison to the non-steroidal anti-inflammatory analgesic (NSAIAs) usage in Hail population (apparently normal) in Saudi Arabia (KSA) and their possible impact on chronic kidney disease (CKD) by performing following parameters test discussed below.

PATIENTS AND METHODS

Baseline study

We have grouped five criteria from apparently normal population of Hail regions (Al-Zahra, Sidian, Sharaf, Alwesitaa, Lubda, Nasia, Nugra, and Samra) for studying analgesics and herbs usage with reference to chronic kidney disease (CKD). The study was performed under the following guidelines for data collection and avoiding individual variations and data validity.

Firstly, different categories of people in Hail were selected for screening CKD distribution. In these Hail regions, the effect of analgesics and herbal drugs were tabulated by simple random sampling.

The first criterion selection was based on gender. The usage of analgesics and herbal on sex was analyzed by the statistical tool, chi-square test. A total of 4565 subjects were selected randomly (Table 1).

Table 1 The gender sample populations selected form Hail region

Sex	Sample Population
Male	2134
Female	2431
Total	4565

The second criterion was based on age, i.e., <25 years to >71 years. The age wise effect of analgesics and herbal drugs was analyzed by chi-square test. A total sample size of 4565 from different age groups of the total population in the Hail was selected to monitor CKD distribution (Table 2).

Table 2 The different age groups and sample size selected form Hail region

Age Groups	Sample Population
<25 Years	1187
26-40 Years	1393
41-55 Years	1160
56-70 Years	693
>71 Years	132
Total	4565

The third criterion was creatinine level in the Hail region. Analgesics and herbal effect on both normal level and high level of creatinine in the population were tabulated by chi-square test. A sample size of 3055 was evaluated for creatinine levels indexing in the area associated with CKD (Table 3).

Table 3 The creatinine levels and sample populations selected form Hail region

Creatinine	Sample Population
Normal	2950
High	105
Total	3055

The last criterion was education level in the Hail region. The use of analgesics/herbal drugs was screened in literate and illiterate populations. A sample size of 4378 was taken from the population and effect of analgesics and herbal drugs was recorded statistically (Table 4).

Table 4 The education levels and sample size selected form Hail region

Education	Sample Population
Illiterate	979
Read And Write	334
Primary	469
Middle	467
Secondary	991
Higher	1138
Total	4378

Ethical Consent

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

Statistical Analysis

Statistics were reported by region, age-group, gender, creatinine and education levels. The observations for analgesics and herbal drugs were calculated using SPSS computer software version 18, cross-tabulation and chi-square test χ^2 statistical analysis. Pearson's chi-square was used with $p<0.05$, which was considered as statistically significant.

RESULTS

In this study, data was collected from apparently normal population of Hail regions (Al-Zahra, Sidian, Sharaf, Alwesitaa, Lubda, Nasia, Nugra, and Samra) on the basis of gender, age, creatinine level, and education levels. The relations were studied by chi-square test.

We have grouped five criteria from a total population of Hail regions, for studying analgesics and herbs effect with reference to chronic kidney disease (CKD). The study was performed under the following guidelines for correct data collection and avoiding individual variations and data validity. In the Hail region, the effect of analgesics and

herbal drugs were tabulated by simple random sampling. A total of 4565 samples from the population were selected randomly. Out of total 4565 samples, 156 (8.798%) have used analgesics and 216 (12.182%) have used herbal drugs. So in the region-based study, the effect of the herbal drug was used more over analgesics with reference to CKD (Hail). The data is shown below in Table 5 for analgesics and herbal drugs.

Table 5 Use of analgesics and herbal drugs

Drugs used	Total
Analgesics	156
Herbal	216

Gender Wise Distribution

In gender wise study, the cross-tabulation table was first prepared for both analgesics and herbal drugs with reference to CKD (HAIL). Then results were commutated by chi-square test (Table 6 and Figure 1).

Table 6 Gender wise distribution of population using and not using analgesics drugs

Sex	Analgesics		Total
	Yes	No	
Male	30	855	885
Female	126	762	888
Total	156	1617	1773

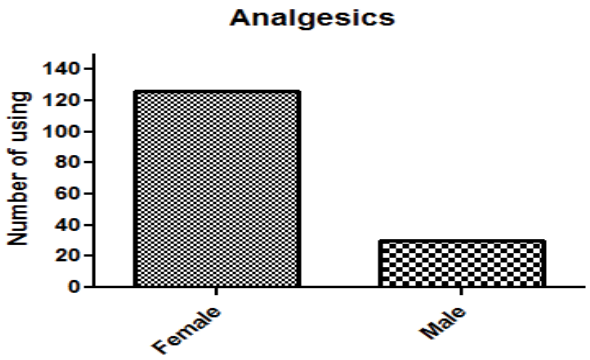

Figure 1 Gender wise distribution (analgesics)

Analgesics

For analgesics drug study of total 1773, 885 male samples were selected out of which only 30 have used analgesics drug. For total 888 female samples selected only 126 have used analgesics drug rest 762 has not used. Out of total 1773 samples, 156 samples have used analgesics drug and 1617 did not use. Around 14.18% female populations have used analgesics, whereas only 3.38% male population used analgesics drugs. Hence, the female population used the analgesics drug more than the male population.

Since the p-value is less than significant α=0.05, we can conclude that there was a significant association between gender and analgesics drug ($\chi^2(1)=68.613$, $p<0.001$).

Herbal

For herbal drug study, total 1773 samples were collected out of which 885 male samples were selected, where only 68 showed to have used herbal drugs while the rest of the sample didn't used. For total 888 female samples selected, only 148 used herbal drugs. Out of total 1773 samples, 216 samples have used herbal drugs while 1557 didn't respond for the herbal drug. About 7.68% of the male population has used herbal drugs while 16.667% female population has used herbal. Females used herbal drugs more than males. Overall response to the herbal drug from total population was more as compared to analgesics drug with reference to CKD (Hail). The female population showed more consumption for both drugs than the male population. However, in overall, herbal drugs were more frequently used than analgesics in case of both genders with reference to CKD.

Since the p-value is less than significance level α=0.05, we can conclude that there was a significant association between gender and herbal drug ($\chi^2(1)=50.700$, $p<0.001$) (Table 7, Figure 2).

Table 7 Gender wise distribution of population using and not using herbal drugs

Sex	Herbal		Total
	Yes	No	
Male	68	817	885
Female	148	740	888
Total	216	1557	1773

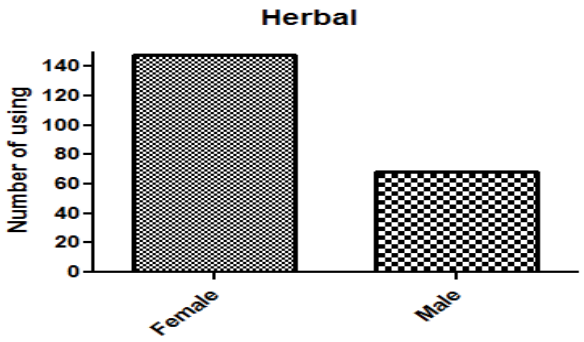

Figure 2 Gender wise distribution (herbal)

Age Wise Distribution

In age group study, the cross-tabulation table was first prepared for both analgesics and herbal drugs with reference to CKD (HAIL). Then results were commutated by chi-square test (Table 8, Figure 3).

Table 8 Age wise distribution of population using and not using analgesics drugs

Age	Analgesics		Total
	Yes	No	
<25 years	13	473	486
26-40	41	501	542
41-55	50	383	433
56-70	47	211	258
>71	5	49	54
Total	156	1617	1773

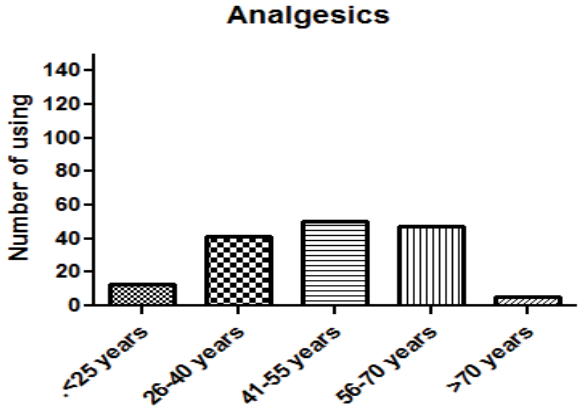

Figure 3 Age wise distribution (Analgesics)

Analgesics

In the analgesics drug study, total 486 samples were selected and following results were observed:

- For age less than 25 years, 13 have used analgesics drugs whereas 473 have not used.
- For the age group between 26-40 years, 41 have used and 501 have not used.
- For the age group between 41-55 years, 50 have used and 383 have not used.
- For the age group between 56-70 years, 47 have used and 211 have not used.
- For age above 71 years, 5 have used and 49 have not used.

So out of total 1773 samples, 156 have used and 1617 have not used analgesics drugs. Samples with age between 41-55 years showed more use of analgesics (11.51%) with reference to CKD (Hail).

Since the p-value is less than significance level $\alpha=0.05$, we can conclude that there was a significant association between age groups and analgesics drug ($\chi^2(4)=56.299$, $p<0.001$).

Herbal

In the herbal drug study, total 1773 samples were selected and following results were observed:

- For the age group less than 25 years, 13 have used the herbal drug and 473 have not used.
- For the age group between 26-40 years, 63 have used and 479 samples have not used the herbal drug.
- For age between 41-55 years, 82 have used and 351 have not used the herbal drug.
- For age between 56-70 years, 51 have used and 207 have not used the herbal drug.
- For age above 71 years, 7 have used and 47 showed to have not used the herbal drug.

Out of total 1773 samples, 216 samples have used and 1557 have not used the herbal drug. Samples with age between 41-55 years showed the use of more herbal products (19.06%) with reference to CKD (Hail). But an overall use of the herbal drug from the total population was more as compared to analgesics drug. Our study shows that according to ascending order of age the number of people are increasingly using the analgesics/herbal drugs (Table 9, Figure 4).

Table 9 Age wise distribution of population using and not using of herbal drugs

Age	Herbal		Total
	Yes	No	
<25 years	13	473	486
26-40	63	479	542
41-55	82	351	433
56-70	51	207	258
>71	7	47	54
Total	216	1557	1773

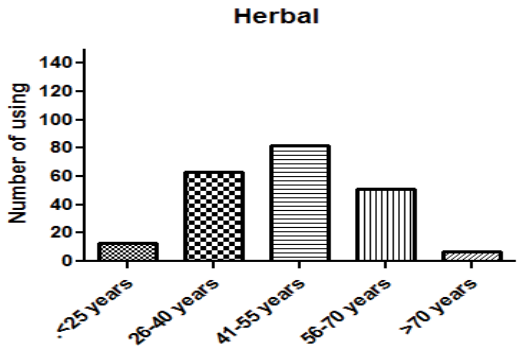

Figure 4 Age wise distribution (Herbal)

Since the p-value is less than significance level α=0.05, we can conclude that there was a significant association between age groups and herbal drug ($\chi^2(4)=47.569$, $p<0.001$).

Creatinine Level

In creatinine level study, the cross-tabulation table was first prepared for both analgesics and herbal drugs with reference to CKD (HAIL), and then results were commutated by chi-square test (Table 10, Figure 5).

Table 10 Creatinine level wise distribution of population using and not using of analgesics drugs

Creatinine level	Analgesics		Total
	Yes	No	
Normal	127	856	983
High	2	33	35
Total	129	889	1018

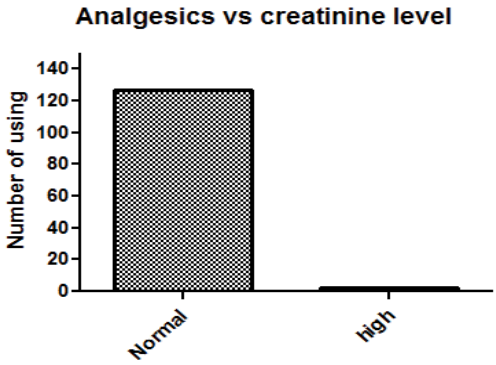

Figure 5 Creatinine wise distribution (Analgesics)

Analgesics

For analgesics drug study, total 1018 samples were collected, 129 showed to have used analgesics drug and 889 have not used. For total 129 samples, 2 showed high creatinine level and 127 showed normal creatinine levels. So out of total 1018 samples, 1.55% of those of high creatinine levels have used analgesics.

Herbal Drug

For herbal drug study, total 1018 samples were collected, out of which 108 showed to have used herbal drugs and 910 have not used herbal drugs. For total 35 samples, 2 showed high creatinine level. So out of total 1.85% of those of high creatinine levels have used herbal drugs. However, overall response for the herbal drug from total population is more as compared to the analgesics drug (Table 11, Figure 6).

Table 11 Creatinine level wise distribution of population using and not using of herbal drugs

Creatinine Level	Herbal		Total
	Yes	No	
Normal	106	877	983
High	2	33	35
Total	108	910	1018

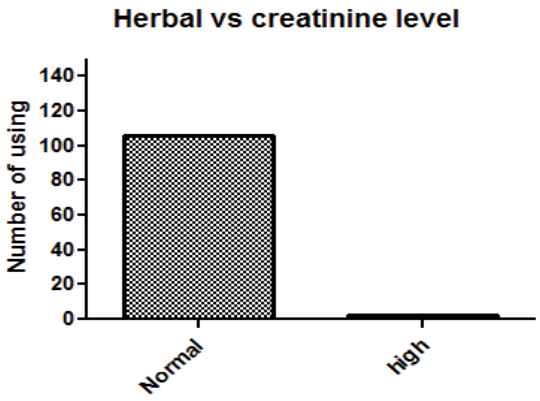

Figure 6 Creatinine wise distribution (Herbal)

For herbal drug, the p-value is more than significance level α=0.05, we can conclude that there was no significant association between creatinine level and herbal drug ($\chi^2(4)=2.274$, $p>0.794$).

For creatinine vs. gender study, total 1019 samples were collected, 364 male samples were selected, out of which 32 showed high creatinine level and 332 showed normal levels. For total 655 female samples selected, 3 showed high creatinine level and 652 showed normal levels. So out of total 1019 samples, 8.79 % of those in the male population have high creatinine levels while 0.45 % of those in the female population have high creatinine levels (Table 12, Figure 7).

Table 12 Gender wise distribution for creatinine level

Sex	Creatinine Level		
	Normal	High	Total
Male	332	32	364
Female	652	3	655
Total	984	35	1019

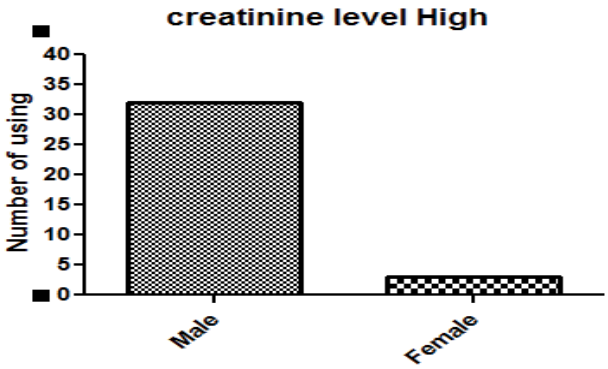

Figure 7 Gender creatinine level

For creatinine vs. age study, total 1019 samples were collected and the following results were observed:

- About 215 sample of age less than 25 years were selected, out of which 3 have high creatinine level and 212 have normal creatinine level.
- For age between 25-40 years, 7 showed high creatinine level and 302 showed normal creatinine level.
- For age between 41-55 years, 10 showed high creatinine level and 284 showed normal creatinine level.
- For age between 56-70 years, 13 have high creatinine level and 164 have normal creatinine level.
- For age above 71 years, 2 have high creatinine level and 22 have normal creatinine level.

So out of total 1019 samples, 35 samples have high creatinine level and 984 have normal creatinine level. Samples with age >71 years have high creatinine level (8.34%) in comparison with different age groups. Our study shows that according to ascending order of age the number of people is also increasing the use of analgesics/herbal drugs and its consequence is also shown in there increasing the order of creatinine levels (Table 13, Figure 8).

Table 13 Age wise distribution for creatinine level

Age	Creatinine Level		
	Normal	High	Total
<25	212	3	215
25-40	302	7	309
41-55	284	10	294
56-70	164	13	177
>71	22	2	24
Total	984	35	1019

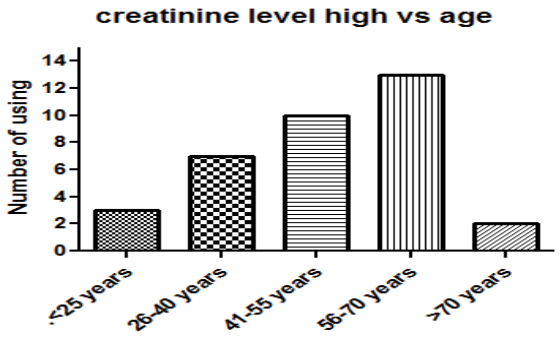

Figure 8 Age vs creatinine level

Education Wise Distribution

In education wise distribution study, the effect of analgesics and herbal drugs with reference to CKD (HAIL) was studied.

- From illiterate population samples, total 362 samples were taken, out of which 66 have used analgesics and 85 used herbal drugs.
- For those that can read and write, out of total 132 samples, 24 have used analgesics and 47 used herbal drugs.
- Samples with primary level education, out of total 175 samples 18 have used analgesics and 16 used herbal drugs.
- Samples with the middle-level education, out of total 182 samples 9 have used analgesics and 17 used herbal drugs.
- Samples with secondary level education, out of total 396 samples 17 have used analgesics and 13 used herbal drugs.
- Samples with higher level education, out of total 450 samples 15 have used analgesics and 23 used herbal drugs.

Out of total 1697 samples, 149 (8.78 %) have used analgesics and 201 (11.84%) used herbal drugs. In education wise distribution study, the use of the herbal drug is more than analgesics in samples with reference to CKD (Hail).

So in our present study, out of total 450 literate we found that highly literate group 3.33% has used analgesics, while 5.11% have used herbal drugs. Among illiterate total 362 samples were selected, 18.23% showed to have used analgesics, while 23.48% showed to have used herbal drugs. Hence, educated people are taking fewer analgesics/ herbal drugs as compared to illiterate. The data is tabulated above in table for analgesics and herbal drugs. So it is clear from our study that education level affects the number of people who used analgesics and herbal drugs.

DISCUSSION

Hail region (northern Saudi Arabia) was populated with more than 500,000 people and in this community-based study a total 4565 samples were taken, in which herbal drugs were more used (12.182%) than analgesics drug (8.798%) [13]. On comparing different regions individually with same sample size, herbal drugs were found to be more used than analgesics with reference to CKD (Hail). The $p<0.001$ (significance level $\alpha=0.05$), also conclude that there was a significant association between age groups and use of herbal products. Relatively similar findings were previously reported from the same area [23].

In gender-wise distribution study, male and female two categories were taken. Out of the total sample population of 1773, herbal drugs were used more among females (12.18%) than analgesics drugs (8.79%). The male population showed 3.38% of usage for analgesics and 7.68% for herbal. The female population showed 14.18% of usage for analgesics and 16.667% for herbal. The female population showed more consumption for both drugs than the male population. However, herbal drugs were more frequently used than analgesics in case of both genders with reference to CKD (Hail). The $p<0.001$ (significance level $\alpha=0.05$), also conclude that there was a significant association between gender and herbal drug. Comparatively such results were previously reported from the same area [23].

In age-wise distribution study, total 1773 sample population was selected from different age groups. Herbal drugs were more used (12.18%) than analgesics drugs (8.79%). Age group below 25 years showed 2.67% for analgesics drugs and 2.67% for herbal drugs. Age group between 26-40 years showed 7.56% for analgesics and 11.62% for herbal. Age group between 41-55 years showed 11.54% for analgesics and 18.93% for herbal. Age group between 56-70 years showed 18.21% for analgesics and 19.76% for herbal. Age group above 70 years showed 9.25% for analgesics and 12.96% for herbal. We can conclude that age group between 41-55 years showed more consumption for both drugs in comparison to other age groups. However, by evaluating different age groups individually for the effect of both drugs, herbal is found to be more used with reference to CKD (Hail). Our study shows that according to ascending order of age the number of people is also increasingly using the analgesics/herbal drugs.

The $p<0.001$ (significance level $\alpha=0.05$), also conclude that there was a significant association between age and herbal drug. Relatively similar findings were previously reported from the same area [24].

In creatinine level indexing study, normal and high level of creatinine was selected. Out of the total sample population 1018, analgesics drugs were more used (12.47%) than herbal drugs (10.41%). High creatinine level shows 1.55% for analgesics and 1.85% for herbal. However, in overall herbal drugs shows a high level of creatinine than analgesics with reference to CKD (Hail). The value of $p>0.132$ (significance level $\alpha=0.05$), conclude that there was no significant association between creatinine level and using analgesics drug in Hail population. However, the increased values of creatinine are always linked to impairment of kidney functions [25,26].

In education wise distribution study, out of the total 1697 sample population selected from different education levels, herbal drugs was used more (11.84%) than the analgesics drug (8.78%). In the read and write groups, analgesics uses were 18.18% and that of herbal was 35.60%. In primary level studied groups, analgesics uses were 10.28% and that of herbal was 9.14%. In middle level studied groups, analgesics uses were 4.94% and that of herbal was 9.34%. In secondary level studied groups, analgesics uses were 4.29% and that of herbal was 3.28%. In higher level studied groups, analgesics uses were 3.33% and that of herbal was 5.11%. We can conclude that out of total 450 literate samples selected in a highly literate group 3.33% have used analgesics, while, 5.11% have used herbal. Among total 362 illiterate samples selected, 18.23% showed to have used analgesics, while, 23.48% showed to have used herbal drugs. However, on comparing education levels individually with same sample size, herbal drugs were found to be more used than analgesics with reference to CKD (Hail). However, more educated people are taking fewer drugs as compared to illiterate. So it is clear from our study that education level affects the number of people who used analgesics and herbal drugs. The $p<0.001$ (significance level $\alpha=0.05$), also conclude that there was a significant association between education and analgesics/herbal drug.

After conducting a study on the population of the Hail region of Saudi Arabia by dividing it into various subgroups i.e. based on gender, age, creatinine level, and education level it can be concluded that growing prevalence of CKD in the Hail regions and increasing use of traditional herbal therapy and NSAIAs improve our knowledge against CKD. However, due to lack of evidence from clinical trials traditional herbal therapies are not supported as safe for use. The toxicities of traditional herbal therapy are unidentified since active components of these herbal drugs are not known [23].

CONCLUSION

As compare to traditional herbal therapy non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used for anti-inflammatory and analgesic properties. The regular use of non-steroidal anti-inflammatory drugs (NSAIDs) for a long period increases the risk of CKD progression. Among literate groups, the drugs were taken in fewer amounts as compared to illiterate ones. Illiterate samples showed a high amount of drug intake for both herbal and analgesics. Hence, educated people are taking lesser drugs as compared to illiterate people. Traditional herbal therapy proves to be more used than analgesics. The use of traditional herbal and NSAIAs is relatively prevalent and associated with CKD confirming the previously reported results [23].

DECLARATIONS

Acknowledgment

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Conflict of Interest

The authors have disclosed no conflict of interest, financial or otherwise.

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