Assessment of Risk Factors for Chronic Kidney Disease in Djamaa (El Oued, Algeria) Population

Samir Derouiche *, Taissir Cheradid, Messaouda Guessoum

Department of Cellular and Molecular Biology, Faculty of the Sciences of Nature and Life, El Oued University, El Oued 39000, El Oued, Algeria

*Corresponding Author: Samir Derouiche
Email: dersamebio@gmail.com

Received: 12 December 2019 / Accepted: 14 February 2020

Abstract

Purpose: This study was conducted aiming at evaluating some risk factors in patients with Chronic Kidney Disease (CKD) in Djamaa (El Oued, Algeria) region.

Materials and Methods: Our study is based on 77 voluntary individuals divided into healthy man and women reserved as a control with average age of 46.61± 2.84 years old and CKD patients with average age of 46.03± 2.95 years old; their origin covers the whole Djamaa (El Oued, Algeria) region and they were selected from the dialysis service of SAAD DEHLEB hospital Djamaa (El Oued Algeria). Risk of certain socio-clinical factors has been estimated by the determination of the value of Odd Ratio (OR).

Results: Our study reports show a strong association between clinical factors such as Diabetes, urinary problems and Arterial hyper pressure (OR= 5.135, 6.60 and 78.276; P ≤0.05) with chronic kidney disease, respectively, but in this study we show that the Renal herbal medicine and History of kidney disease are the most dangerous risk factors, (OR = 20.00, OR =25.45 ; p≤0.001), respectively, for spices and Amount of water (OR ranging from 0.232 to 0.352; P ≤0.032) are important protective factors against this disease.

Conclusion: Lifestyle is a contributing factor in CKD attainment in the region of Djamaa (El Oued, Algeria), which requires high sensitivity to modify these behaviors for limited progression of the disease in this region.

Keywords: Chronic Kidney Disease; Risk Factors; Protective Factors; Djamaa.
1. Introduction

Chronic Kidney Disease (CKD) is a real public health problem because its prevalence is increased in the international population and its effect on the mortality rate among patients with it [1]. The incidence of chronic renal failure in Algeria has been estimated as 34 per million people per year. This amounts to nearly 1000 new patients each year [2]. Also, large numbers of this disease have been recorded in different regions of Algeria, especially the desert ones, such as a Djamaa region, which is known as a remarkable increase in the number of patients, which constituted a clear threat to public health. Nevertheless, the real reasons for this remarkable increase in the disease (CKD) are not yet known, especially in this desert region. This region is known also for its great agricultural activity and for its high salinity water quality. Chronic renal failure is characterized by the decrease in glomerular filtration rate diagnosed by the increased excretion of albumin in the urine which has become an important public health problem [3] with 8-16% prevalence at baseline world level. According to 2002 statistics, still in this year (2002), the clinical practice guidelines of the Quality Initiative for the Effects on Kidney Disease of the US National Kidney Foundation [4] this organization defines the disease as a renal impairment or a glomerular filtration rate less than 60 mL / min for 1.73 m² for more than 3 months, it proposed a classification system based on glomerular filtration rate [5]. However, the reported prevalence of this chronic disease is varied across countries due to several factors such as age, survey policies, ethnic groups and DFG6 calculation equations [6]. The characteristics of risk factors and targeting strategies are also very diverse [7]. Faced with this problem, and in the absence of statistics or scientific study on this disease and its risk factors in these regions of Algeria, this study aims at identifying the factors associated with chronic kidney disease in relation to levels of socioeconomic development and health-care systems in individuals of the Djamaa (El Oued, Algeria) population who have undergone hospitalization in a public hospital.

2. Materials and Methods

2.1. Subject of Study

Ethical approval was requested and approved by the ethics committee (12 EC/DCMB/FNSL/EU2019) of the department of cellular and molecular biology, faculty of natural sciences and life, University of El Oued. Our study was based on 77 voluntary individuals divided into healthy people reserved as a control (n=41) with average age of 46.61±2.84 years old and chronic kidney disease patients (n=36) with average age of 46.03 ± 2.95 years old. In this study, we divided the subjects into two groups according to the simple randomization method. All of the volunteers (control and patients) in this study live in the Djamaa (El Oued) area located in the south east of Algeria. Therefore, their social and demographic information, including age, sex, weight, social case, job, educational level, and blood group were collected by completing the questionnaires from their medical records or through a direct discussion with patients. In the questionnaires, we relied on many variables, which can be the cause of the disease, including Clinicopathological variables such as excessive use of drugs products, chronic diseases like HTA, Rheumatism and Diabetes, using drugs (automedication), excessive use of antibiotic and people with urinary problem or history kidney disease. There are also other variables related to social behaviors of people such as drinking a lot of water, excessive drinking of tea or soft drinks, using spices and renal herbal medicine, playing sport, excessive eating of sweet or salty foods, working in farms.

2.2. Inclusion and Exclusion Criteria

Inclusion criteria for Chronic Kidney Disease (CKD): clinical diagnosis shows CKD suffering for three months confirmed by specialist doctors, also patients receiving dialysis but no other type of chronic disease treatment for 30 days. Regarding the control group, the participants are healthy people not suffering from chronic or acute diseases and consume no drug for 30 days. Exclusion criteria were to eliminate all other types of kidney diseases.
2.3. Statistical Analysis

Values were expressed as percent per population or as the Mean ± Standard Deviation (SD). Data were presented using frequency tables. Chi-square test was used to test for association between risk factors and Chronic Kidney Disease (CKD). Relative risks and Odds ratios were calculated by Cochran's and Mantel Haenszel statistics using SPSS 16. Odds ratios >1 and P<0.05 indicate a significant risk factor. OR<1 and P<0.05 indicate a significant protective factor.

3. Results

3.1. Description of Study Population

The population of our study are characterized by many different characters (age, weight, sex, social case, job, education level, blood group). This population are recruited by hemodialysis service, they are represented Chronic Kidney Disease (CKD) confirmed by the diagnosis kidney echography and nephrologists doctors of hospital SAAD DAHLEB, Djamaa. In our study we selected 36 hemodialysis patients and 41 controls; after statistical analysis we obtained the results which are presented in Table 1.

3.2. Study of Socioeconomic and Clinic Factors

Odds Ratio (OR) values for Socioeconomic factors (Table 2) and Clinicopathological factors (Table 3) show that diabetes, urinary problems and hypertension are shown to be significant risk factors for chronic kidney disease (OR= 5.135; P= 0.003), ( OR= 6.607; p=0.001), ( OR= 8.276; P= 0.000 ), respectively. In addition, Rheumatism ( OR= 14.375; P= 0.004 ), History of kidney disease (OR= 20.000; P= 0.000 ) and Renal herbal medicine (OR=25.455; P= 0.000) are also very important risk factors of chronic kidney disease in our study population by highest OR values. While spices, amount of water, and salty foods are protective factors for Chronic Kidney Disease (CKD) in the study population (OR ranging from 0.232 to 0.352; P ≤0.032), in contrast, our results indicate that tea, coffee, food additive, sweet foods, antibiotic and drug products are not considered as predictors of Chronic Kidney Disease (CKD) in our population since the obtained OR values are not significant.

### Table 1. Description of study population

|               | Control (N=41) | Patients (N=36) |
|---------------|----------------|-----------------|
| Age           | 46.61 ± 2.84   | 46.03 ± 2.95    |
| Body Weight   | 61.20 ± 2.09   | 59.96 ± 2.62    |
| Sex           |                |                 |
| Men %         | 16.88          | 23.38           |
| Women %       | 36.36          | 23.38           |
| Social Case   |                |                 |
| Married %     | 29.870         | 29.870          |
| Single %      | 23.376         | 15.584          |
| Job           |                |                 |
| Worker %      | 19.480         | 14.285          |
| Unemployed %  | 33.766         | 32.467          |
| Educational Level |         |                 |
| Primary %     | 5.194          | 25.974          |
| Medium %      | 7.792          | 5.194           |
| High school % | 19.480         | 12.987          |
| High education % | 20.779   | 2.597           |
| Blood Group   |                |                 |
| A %           | 18.181         | 7.791           |
| B %           | 10.389         | 10.388          |
| AB %          | 7.791          | 3.896           |
| O %           | 16.882         | 18.181          |
Table 2. Comparison of the Socioeconomic factors of CKD patients and control (N= 77)

| Factor              | Control % | Patient % | OR     | CI95%   | P-value  |
|--------------------|-----------|-----------|--------|---------|----------|
| Amount Water       |           |           |        |         |          |
| Positive           | 48.051    | 25.974    | 0.362  | 0.143-0.913 | 0.025    |
| Negative           | 7.792     | 20.779    |        |         |          |
| Tea                |           |           |        |         |          |
| Positive           | 18.181    | 15.584    | 0.893  | 0.344-2.326 | 0.504    |
| Negative           | 32.467    | 31.168    |        |         |          |
| Spices             |           |           |        |         |          |
| Positive           | 36.363    | 15.584    | 0.232  | 0.89-0.604 | 0.002    |
| Negative           | 18.883    | 31.168    |        |         |          |
| Food additive      |           |           |        |         |          |
| Positive           | 12.987    | 7.792     | 0.620  | 0.200-1.919 | 0.292    |
| Negative           | 40.259    | 38.969    |        |         |          |
| Additive soft drinks |         |           |        |         |          |
| Positive           | 25.974    | 11.88     | 0.350  | 0.132-0.925 | 0.027    |
| Negative           | 27.272    | 35.064    |        |         |          |
| Renal herbal medicine |        |           |        |         |          |
| Positive           | 1.298     | 18.181    | 25.455 | 3.135-206.705 | 0.000    |
| Negative           | 51.948    | 28.571    |        |         |          |
| Sport              |           |           |        |         |          |
| Positive           | 25.974    | 16.883    | 0.593  | 0.238-1.482 | 0.187    |
| Negative           | 27.272    | 29.870    |        |         |          |
| Sweet Food         |           |           |        |         |          |
| Positive           | 29.870    | 16.883    | 0.442  | 0.177-1.108 | 0.063    |
| Negative           | 23.376    | 29.870    |        |         |          |
| Salty Food         |           |           |        |         |          |
| Positive           | 22.077    | 9.090     | 0.341  | 0.121-0.957 | 0.032    |
| Negative           | 31.168    | 37.662    |        |         |          |
| Works Agricultures |           |           |        |         |          |
| Positive           | 10.390    | 2.597     | 0.243  | 0.048-1.228 | 0.067    |
| Negative           | 42.857    | 44.155    |        |         |          |

Table 3. Comparison of the Clinicopathological factors of CKD patients and control (N= 77)

| Factor              | Control % | Patient % | OR     | CI95%   | P-value  |
|--------------------|-----------|-----------|--------|---------|----------|
| Drugs products     |           |           |        |         |          |
| Positive           | 1.298     | 6.493     | 0.258  | 0.029-2.324 | 0.199    |
| Negative           | 51.984    | 40.259    |        |         |          |
| Hypertension       |           |           |        |         |          |
| Positive           | 5.194     | 22.077    | 8.276  | 2.439-28.079 | 0.000    |
| Negative           | 48.059    | 24.675    |        |         |          |
| Diabetes           |           |           |        |         |          |
| Positive           | 6.493     | 10.389    | 5.134  | 1.6346-16.182 | 0.003    |
| Negative           | 46.753    | 36.363    |        |         |          |
| Using drugs        |           |           |        |         |          |
| Positive           | 25.974    | 18.181    | 0.668  | 0.270-1.656 | 0.261    |
| Negative           | 27.272    | 28.571    |        |         |          |
| Antibiotic         |           |           |        |         |          |
| Positive           | 9.090     | 11.688    | 0.462  | 0.181-1.179 | 0.283    |
| Negative           | 44.155    | 35.064    |        |         |          |
| Rheumatism         |           |           |        |         |          |
| Positive           | 19.480    | 25.974    | 14.375 | 1.670-123.701 | 0.004    |
| Negative           | 33.766    | 20.779    |        |         |          |
| Urinary problem    |           |           |        |         |          |
| Positive           | 5.194     | 19.480    | 6.607  | 1.939-22.516 | 0.001    |
| Negative           | 48.051    | 27.272    |        |         |          |
| History kidney disease |       |           |        |         |          |
| Positive           | 1.298     | 15.584    | 20.000 | 2.445-163.622 | 0.000    |
| Negative           | 51.948    | 31.168    |        |         |          |
4. Discussion

Our study shows that the diabetes and hypertension are the principal causes for the Chronic Kidney Disease, as study of Hwang et al. (2010) [8], which was based on NHI data, showed that diabetes and hypertension were associated with a higher risk of developing Chronic Kidney Disease (CKD). Diabetes mellitus (43.2%) and hypertension (8.3%) are major underlying renal disease of End Stage Renal Disease (ESRD) in 2007. According to the registry of Turkish society of nephrology, diabetic patients constitute 37.3% of hemodialysis population in turkey and depending on the USRDS data, half of the new ESRD patient in the United States have diabetic nephropathy [9]. So, diabetes mellitus has become the first leading cause of ESRD by outnumbering Chronic Glomerulonephritis (CGN) since 2000 [8]. Approximately 30% of patients with diabetic nephropathy eventually progress to end-stage renal failure, and the rest usually die from cardiovascular disease before reaching the end stage [10]. The relationship between hypertension and renal disease is shown in a direct consequence of altered renal development and progression loss of kidney function if hypertension is superimposed on intrinsic kidney disease [11]. Some chronic illnesses, such as diabetes, serve as independent risk factors of cancers and other diseases may be associated with mortality [12]. It is possible that diffuse arteriosclerosis, which is associated with hypertension can have a direct influence on the kidney to decrease filtration and indirect influence on the kidney by the way of decreased diffusion which can result in elevated creatinine level and increased risk [13].

Concerning rheumatoid arthritis we arrived rheumatoid arthritis is higher risk factor for Chronic Kidney Disease, as in study of Karie et al., (2008) [14] who said the Chronic Kidney Disease was highly prevalent in there population of RA patients, nearly half of RA patients are presenting a kidney disease according to National Kidney Foundation–Kidney (NKF) classification. In addition, Hsien-Yi Chiu et al., (2015 ) [15] study investigated the cause of renal disease in Rheumatoid Arthritis (RA) patients; it demonstrates that the risk of the development of the CKD, GN and ESRD are attributable to nephrotoxic pharmacotherapy and chronic inflammatory state as demonstrated by elevation of various growth factors, inflammatory mediators, and/or inflammatory markers, such as C-Reactive Protein (CRP), interleukin-6, Tumor Necrosis Factor alpha (TNF-α) and renal amyloidosis [16].

The study of LaTony et al. (2014) [17] is combined between Rheumatoid Arthritis (RA) disease characteristics and Cardiovascular Disease (CVD) associated factors which appear to play a role in reduced kidney function

Our study showed that the urinary problems and History of kidney disease are health risk factors for Chronic Kidney Disease. Staghorn calci, urinary infection and impairment of renal function are at risk of development of terminal renal failure glomerulonephritids, interstitial nephritis and polycystic KD [18, 19]. Urinary Tract Infection (UTI) is a bacterial infection of the urine (> 105 colony-forming units/ml of urine), which may involve the kidney (pyelonephritis) whose patients have an increased risk of associated kidney damage scarring which can result in renal failure [20]. Pyelonephritis is still one of the major causes of ESRD although bacterial infection has become of lesser importance in this respect in the last 10-15 years [18]. According to Kidney Foundation of Canada (2015), kidney stone can develop when certain chemicals in the urine from crystals that stick together, larger stones may block the flow of urine or irritate the liming of the urinary tract [21]. The risk factors of CKD are characterized by multiple cysts in both kidney [22]. Glomerulonephritis stands out as the major cause of renal failure. However the alternative in progressive forms of glomerulonephritis is death from renal failure [23]. Colín L. et al. (1992) concluded that tubulo-interstitial nephritis describes a range of pathological processes that are at least partly responsible for progression of renal disease of nearly all etiologies [24]. According to Choi Y. J. et al. (2000), Chronic Tubule-interstitial Injury (CTI), including tubular atrophy and interstitial fibrosis represents one major determinant for the progression renal chronic disease regardless of cause [25]. Nephrosclerosis is an umbrella term defining changes in all compartments of the kidney. These lesions are accompanied by tubule-interstitial inflammation and fibrosis that predict the decline of
renal function [26]. With regard to disease before CKD, they are higher risk factors for Chronic Kidney Disease (CKD) as the study of Eleftheria et al. (2014) showed the major causes of End-stage renal disease (ESRD) were diabetic nephropathy (19.5%), hypertensive nephropathy (13.8%), and chronic interstitial nephritis (11.4%). In addition, we obtained that the renal herbal medicine is important risk factor for the Chronic Kidney Disease [19]. In the study of Bagnis et al. (2004), herbal medicine may be a risk for the kidneys; various renal syndromes were reported after the use of medicinal plants. Powdered plant extracts may be intentionally adulterated by other drugs [27]. As an example, a case of analgesic nephropathy was observed in Malaysia after the long-term use of traditional Chinese herbal preparations [28]. The active Principe of herbal drugs derived from aristolochia species is Aristolochic Acid (AA) which was shown to be nephrotoxic in humans and rabbits [29]. The study of Perazella (2009) shows that Renal injury and clinical renal failure can occur through a variety of mechanisms after administration of different therapeutic agents. Also, most forms of parenchymal kidney injury can progress to Chronic Kidney Disease [30]. Focusing on chronic tubulointerstitial nephritis, several agents are more commonly associated with Chronic Kidney Disease, including combination analgesics (phenacetin, NSAIDs, caffeine), 5-amino-salicylic acid (mesalamine), aristolochic acid-containing herbal remedies [31]. Our result showed that spice is a protective factor for Chronic Kidney Disease. According to Fazel et al. (2011), Curcumin treatment at the doses of 10 and 20 mg/kg (intraperitoneally) showed significant nephroprotective effects [32]. The results of Bayrak et al. (2008) study showed that Curcumin through an antioxidative activity effectively salvaged CsA nephrotoxicity [33]. In the study of Anurag et al. (2007) who said Curcuma treatment significantly and dose-dependently restored renal function, it reduced lipid peroxidation and enhanced the levels of reduced glutathione and activities of superoxide dismutase and catalase [34]. In general, herbs and spice have high antioxidant concentration that has the potential to inhibit the oxidation of LDL [35].

5. Conclusion

Hence, in this study it was found that diabetes, urinary problems, arterial hyper pressure, Rheumatism, History of kidney disease and Renal herbal medicine are shown to be major risk factors for Chronic Kidney Disease, which indicates the importance of social behavior and the clinical factor of Chronic Kidney Disease involvement. In contrast, spices, amount of water and salty foods are protective factors for Chronic Kidney Disease in the study population.

Acknowledgements

The author thanks the staff of laboratory of faculty of natural science and life and the staff of dialysis service of SAAD DAHLEB Hospital for providing research facilities to carry out present work.

References

1- E. Fung, T. M. Kurella. Epidemiology and Public Health Concerns of CKD in Older Adults. Adv Chronic Kidney Dis. Vol. 23(1), pp. 8-11, 2016.

2- H. Salah. An Overview of Renal Replacement Therapy in Algeria. Saudi J Kidney Dis Transp. Vol. 5 pp. 190-2, 1994.

3- V. Jha, G. Garcia-Garcia,k, Iseki, Li Z., Naicker, S., Plattner. B., Saran, R., Wang. A. Y., Yang, C. W. Chronic kidney disease: global dimension and perspectives. Lancet, Vol. 382 (9888), pp. 260-72, 2013.

4- L. Zhang, D. Rothenbacher. Prevalence of chronic kidney disease in population-based studies: systematic review. BMC Public Health, Vol. 8, pp. 117 - ??, 2008.

5- R. J. Glassock, C. Winearls. Ageing and the glomerular filtration rate: truths and consequences. Trans Am Clin Climatol Assoc. Vol. 120, pp. 419-28, 2009.

6- P. Delanaye, R.J. Glassock, H. Pottle, A.D. Rule. An Age-Calibrated Definition of Chronic Kidney Disease: Rationale and Benefits. Clin Biochem Rev. Vol. 37(1), pp. 17-26, 2016.

7- J. Ahern, M.R. Jones, E. Bakshis, S. Galea. Revisiting rose: comparing the benefits and costs of population-wide and targeted interventions. Milbank Q. Vol. 86, no. 4, pp. 581-600, 2008.
11- A.L. Valerie, M.B. Barry. The Clinical Importance of Nephron Mass; Journal of the American Society of Nephrology. 2010. doi: 10.1681/ASN.2009121248.

12- Derouiche S. Arousni N, Guediri S. The Study of Socioeconomic and Clinic Risk Factors of Breast Cancer in Algerian Women Population. Front. Biomed. Tech. Vol. 5(3-4), pp. 51-57, 2018.

13- B.S. Neil, E.F. Charles, H.W. Dallas, M. Donald Blafox, S. David, G. L. Herbert, A. Kenneth. Prognostic Value of Serum Creatinine and Effect of Treatment of Hypertension on Renal Function. Schneider on behalf of the Hypertension Detection and Follow-up Program Cooperative Group. Supplement I Hypertension, Vol. 13(5), pp. 80-93, 1989.

14- S. Karie, F. Gandjbakhch, N. Janus, V. Launay-Vacher, S. Rozenberg, C.U. Mai Ba, P. Bourgeois. Deray Kidney disease in RA patients: prevalence and implication on RA-related drugs management: the MATRIX study. Rheumatology, Vol. 47, pp. 350–354, 2008.

15- H. Chiu, H. Huang, C. Li, H. Chen, C. Ye, S. Chiu, W. Lin, Y. Cheng, T. Tsai, S. Ho. Increased Risk of Chronic Kidney Disease in Rheumatoid Arthritis Associated with Cardiovascular Complications – A National Population-Based Cohort Study. Emmanuel A Burdmann, University of Sao Paulo Medical School, BRAZIL; PLoS ONE, Vol. 10(9), e0136508, 2015. doi:10.1371/journal.pone.0136508.

16- W.K. Hyun, C. Lee, H. Cha, J. Choe, E. Park, J. Kim. Effect of anti-tumor necrosis factor alpha treatment of rheumatoid arthritis and chronic kidney disease. Rheumatol Int. 2014. DOI 10.1007/s00296-014-3146-4.

17- J.H. LaTonya, S.C. Cynthia, E.G. Sherine, T.M James, L.M. Eric. Development of Reduced Kidney Function in Rheumatoid Arthritis. Am J Kidney Dis. Vol. 63(2), pp. 206-213, 2014.

18- K. Holmgren, B.G. Danielson, B. Fellstrom. Infection-induced urinary calculi and renal failure; From the Departments of Urology and Internal Medicine, University Hospital, S-75185 Uppsala. Sweden. Scand J UrolNephrol, Vol. 21, pp. 219-223, 1987.

19- T. Eleftheria, B. Vagia, S. Areti, S. Kostas, R. Michael, Z. Zacharias. Causes and complications of chronic kidney disease in patients on dialysis. Department of Nursing, Technological Educational Institute of Athens; Health Science Journal, Vol. 8(3), pp. 343-349, 2014.

20- M.A. David, A. F. Morey, L.G. Gomella, J.P. Stein. Urinary tract infection: definitions, incidence, and investigations chp 05: Infections and inflammatory conditions. Oxford American Handbook of Urology. Vol. 691, pp. 133-154, 2011.

21- Kidney Foundation of Canada. Living with reduced kidney function; 5th Edition, 2015.

22- G.T. Obrador, U.T. Schultheiss, M. Kretzler. Genetic and environmental risk factors for chronic kidney disease. Kidney Int Suppl. Vol. 7, no. 2, pp.88-106, 2017.

23- P. Kincaid-Smith. The Treatment of Glomerulonephritis; From the Department of Medicine, University of Melbourne and Royal Melbourne Hospital, Victoria. AustN. Z. J. Med. Vol. 10(3), pp.340-345, 1980.

24- L.J. Colin, A.E. Allison. Tubule interstitial nephritis. Pediatr Nephrol. Vol. 6, pp. 572-586, 1992.

25- Y.J. Choi, S. Chakraborty, V. Nguyen, C. Nguyen, B.K. Kim, S.I. Shim, W.N. Suki, L.D. Tuong. Peritubular capillary loss is associated with chronic tubule interstitial injury in human kidney: altered expression of vascular endothelial growth factor. Hum Pathol. Vol. 31(12), pp. 1491-1497, 2000.

26- A. Meyrier. Nephrosclerosis: update on a centenarian ; Université Paris-Descartes, Paris, France and Département de Néphrologie, Hôpital Georges Pompidou (AP-HP), Paris, France.Nephrol Dial Transplant, Vol. 30, pp. 1833–1841, 2015.

27- C.I. Bagnis, G. Deray, A. Baumelou, L.Q. Moglie, J.L. Vanherweghem. Herbs and the Kidney. American Journal of Kidney Diseases, Vol. 44(1), pp. 1-11, 2004.

28- J. Vanherweghem, Misuse of Herbal Remedies: The Case of an Outbreak of Terminal Renal Failure in Belgium (Chinese Herbs Nephropathy). The Journal of Alternative and Complementary Medicine, Vol. 4(1), pp. 9-13, 1998.

29- S. Derouiche, K. Zeghib. Evaluation of the Chelating Efficacy of Aquilaria malaccensis and Aristolochia longa Against Biochemical Alterations Induced by Lead Bioaccumulation in Rats. Pharmaceutical and Biosciences Journal, Vol. 7(2), pp. 11-15, 2019.

30- M.A. Perazella. Renal Vulnerability to Drug Toxicity. Clin J Am Soc Nephrol. Vol. 4, pp. 1275–1283, 2009.
31- R.L. Luciano, M.A. Perazella. Aristolochic acid nephropathy: epidemiology, clinical presentation, and treatment. *Drug Saf*, Vol. 38(1), pp. 55-64, 2015.

32- S.N. Fazel, A.H. Moghaddam, S. Eslami, S.M. Nabavi. Protective Effects of Curcumin against Sodium Fluoride-Induced Toxicity in Rat kidney. *Biological Trace Element Research*, Vol. 145(3), pp. 369-374, 2012.

33- O. Bayrak, U. Ebru, B. Reyhan, T. Faruk, A.F. Atmaca, S. Sahin, E.Y. Mehmet, A. Kaya E. Cimentepe, A. Akcay. Curcumin protects against ischemia/reperfusion injury in rat kidneys. *World J Urol.*, Vol. 26, pp. 285–291, 2008.

34- K. Anurag, P. Sangeeta, S. Sameer, T. Naveen, C. Kanwaljit. Effect of Curcumin on Inflammation and Oxidative Stress in Cisplatin-Induced Experimental Nephrotoxicity. Pharmacology Research Laboratory, University Institute of Pharmaceutical Sciences, UGC Centre for Advanced Studies, Panjab University, Chandigarh-160014, *India J. Agric. Food Chem.*, Vol. 55, pp. 10150–10155, 2007.

35- L.C. Tapsell, I. Hemphill, L. Cobiac, D.R. Sullivan, M. Fenech. Health benefits of herbs and spices: the past, the present, the future. *The Medical Journal of Australia*, Vol. 185(4), pp. S4-24, 2006.