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Research Article

Association of genetic and Biochemical markers with GFR among renal failure patients: Applying Serum Creatinine and Cystatin C measures

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Abstract: To assess the association of genetic and Biochemical markers with GFR among renal failure patients. The method in chronic kidney disease (CKD) was evaluated depending on GFR calculation using Serum Creatinine and Cystatin C equations, using the standardized definition from the Kidney Disease Outcomes Quality Initiative of the National Kidney Foundation (K/DOQI) practice guideline. The results in this study the means ± SD for GFR ml/min/1.73 m^2 using creatinine and statin C were 19.8163 ±1.3068 and 19.6122±1.2461, respectively. Of the 103 patients, 50/103 (48.5%), 33/103(32%) and 20/103 (19.5%) were with GRF levels <15, 16-30 and 31+, respectively. In conclusion Patients with CKD or renal failure have a diverse biochemical values which necessitate the urgent need for implantation of health strategies that can assist in the control of the disease and management of patients with disease.
Keywords: CKD, KSA, renal failure, GFR.

INTRODUCTION

Kidney Failure is the end stage of CKD which is responsible of a number of symptoms. Worldwide, CKD is becoming a frequent disease in the common population. Detection of CKD in distinct groups remains poor, particularly among elderly individuals, females or other ethnic groups such as Asians [1]. CKD is a common disorder that regardless of etiology results in a varied range of complications such as, hypertension, hyperparathyroidism, anemia, vascular calcification and accelerated cardiovascular disease [2, 3].CKD can Progress to kidney failure or other adverse consequences could be prevented or delayed through early detection and treatment of patients with CKD [4].CKD is defined by the National Kidney Foundation [5] as either a decline in glomerular filtration rate (GFR) to <60 ml/min/1.73 m2 or the existence of kidney damage for at least 3 months. Signs of kidney damage classically comprise proteinuria, but other markers of damage, such as persistent glomerulo-nephritis or structural damage from polycystic kidney disease can also be existent [6].

In a recent study from Kingdom of Saudi Arabia (KSA), Prevalence rates of all stages CKD was 9.4%. The GFR estimation was available for 2,946 individuals, among whom, 278/2946 (9.4%) were found with impaired kidney function). Of the 278 individuals with CKD, 11/2946(0.4%), 16/2946(0.5%), 229/2946(7.8%) and 22/2946 (0.6%) were estimated for GFR rates of stage V, Stage IV, stage III and stage IV, in this order. CKD prevalence is high in Hail, KSA; thus, preventive interventions are extremely suggested, since, CKD prevalence is likely to increase over the next decades due to rise of its risk factors [7]. Therefore, the aim of the present study was to assess the association of genetic and Biochemical markers with GFR among renal failure patients in Hail region, KSA.

MATERIALS AND METHODS

This study a multi-center cross sectional survey included 5000 Saudi nominated from 30 primary health care centers (PHCs) in Hail Region, KSA. CKD was evaluated depending on GFR calculation using Serum Creatinine and Cystatin C equations, using the standardized definition from the Kidney Disease Outcomes Quality Initiative of the National Kidney Foundation (K/DOQI) practice guideline, and particularly focus on performance of serum-creatinine based equations for GFR estimation. About 103 patients

with Renal Failure (full coverage) were selected for this study.

Statistical analysis

For all statistical analyses, the SPSS statistical software version 17 was used. Pearson chi square test was used and P. values of 0.05 or less were regarded as statistically significant.

Ethical consent

The study was approved by the College of Medicine, Research Board of Hail University. Each candidate was asked to sign a written ethical consent during the interview before the taking of the sample.

RESULTS

This study investigated 103 patients with renal impairment; their mean ± SD age was 52.4±2.04 years with males': females' ratio of 1.80: 1.00. Although, no significance difference between Serum Creatinine and Cystatin C measures, but we calculate GFR from the two estimations mean. The means ± SD for GFR ml/min/1.73 m^2 using creatinine and statin C were 19.8163 ±1.3068 and 19.6122±1.2461, respectively. Of the 103 patients, 50/103 (48.5%), 33/103(32%) and 20/103 (19.5%) were with GRF levels <15, 16-30 and 31+, respectively as indicated in Fig1.

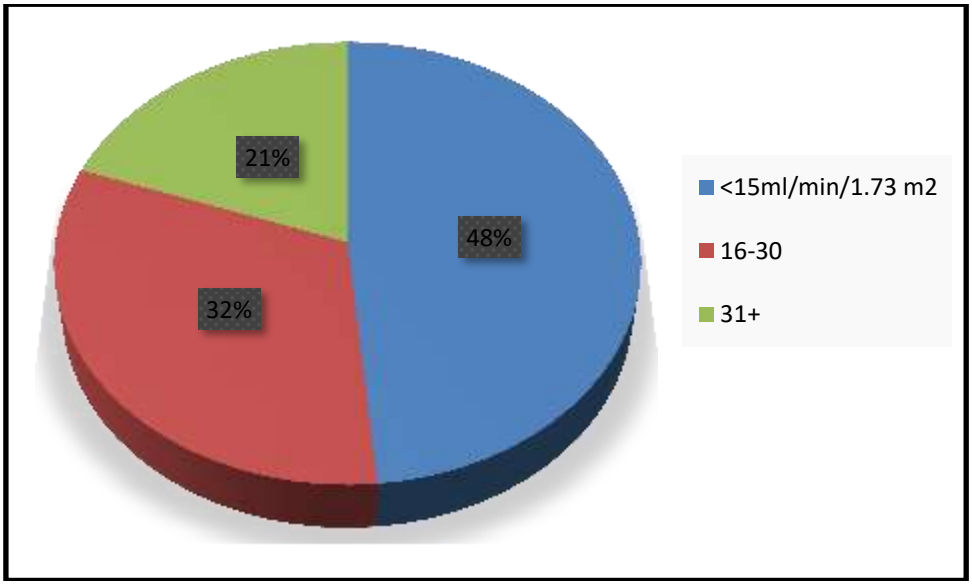

Fig 1: Description of the study population by level of renal impairment (GFR ml/min/1.73 m^2)

The means ± SD for creatinine, urea and uric acid were 397.45±268.874µmol/L, 12.6354±12.0235mmol/L and 188.2±138.7µmol/L, respectively. The means ± SD for Potassium (K), Sodium (Na), Calcium (Ca) and Chloride were; 4.1615±0. 87438 mol/L, 134.612 ±4.43402 mol/L, 2.3243±0.31043 mol/L, and 98.4880±4.45415, in this order, as indicated in Table.1, males represent the great majority of the study population (65.05%). The severity of renal impairment has a gradual increase in number both for males and females for example GFR of 31+, 16-30 and <15, represented (32&18), 23&10), and (12,8) for males & females, in this order as indicated in Table 1 and Fig 2.

Table-1: Distribution of the study population by GFR and sex & age

Variable	Category	GFR ml/min/1.73 m^2			
		<15	**16-30**	**31+**	**Total**
Sex	**Males**	32	23	12	67
	Females	18	10	8	36
	Total	50	33	20	103
Age	**<35yrs**	5	12	5	22
	36-54	9	5	2	16
	55-64	10	10	3	23
	65+	26	6	10	42
	Total	50	33	20	103

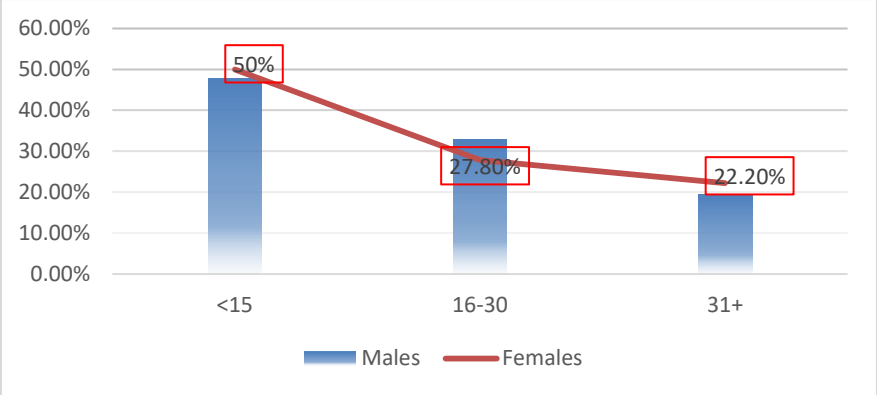

Fig 2: Description of the study population by Sex and GFR levels

Table 2 Showing the distribution of the study population by GFR and genetic and biochemical markers, for genetic analysis of Uromodulin gene analysis, five, one and 3 positive cases were identified in GFR values of <15, 16-30 and 31+, respectively. For creatinine, high creatinine levels were determined in GFR values of <15, 16-30 and 31+, representing 48, 32, and 18 cases respectively. For urea, high urea levels were determined in GFR values of <15, 16-30 and 31+, representing 36, 10, and 10 cases respectively. For uric acid, high uric acid levels were determined in GFR values of <15, 16-30 and 31+, representing 10, 4, and 5 cases respectively. Moreover, low uric acid levels were also found in GFR values of <15, 16-30 and 31+, representing 24, 32, and 8 cases respectively, see Fig 3.

Table2. Distribution of the study population by GFR and genetic and creatinine, urea and uric acid markers

Variable	Category	GFR ml/min/1.73 m^2			
		<15	**16-30**	**31+**	**Total**
Genetic	**Positive**	5	1	3	9
	Negative	45	32	17	94
	Total	50	33	20	103
Creatinine	**Normal**	2	01	2	4
	High	48	32	18	99
Urea	**Normal**	13	26	8	47
	High	36	10	10	56
Uric acid	**Low**	24	32	8	64
	Normal	15	3	2	20
	High	10	4	5	19

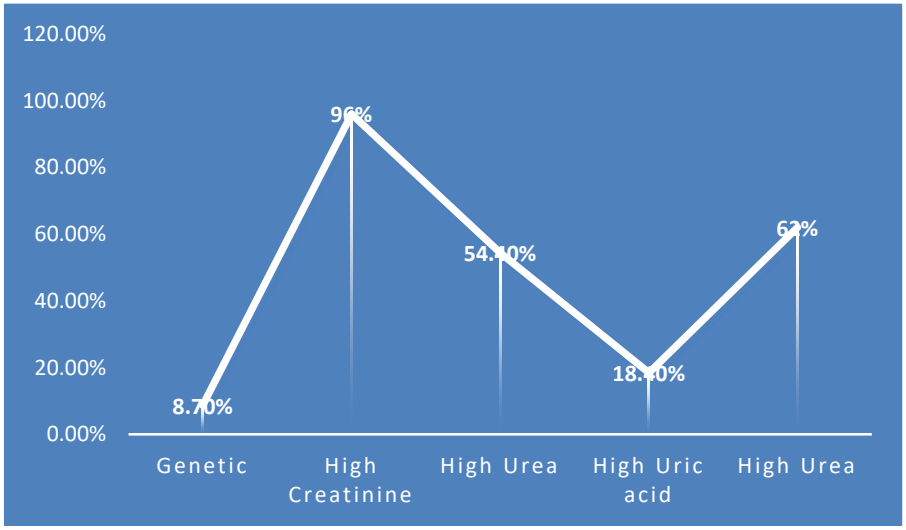

Fig 3: Description of the study population by GFR levels and genetic and biochemical markers

Table 3 summarizes the relationship between GFR levels and minerals, low K+ was measured in 17/103 (16.5%), since high K+ was encountered in 7/103(6.8%). On the other hand low Na+ was identified in 53/103 (51.5%), as well as, low Ca++ was determined in 99/103(96%). Moreover, low and high chloride were identified in 24/103(23.3%) and 5/103 (4.9%), in this order, as indicated in Fig4.

Table 3: Distribution of the study population by GFR and K+, Na+, Ca++, and Chloride markers

Variable	Category	GFR ml/min/1.73 m^2			
		<15	16-30	31+	Total
K+	Low	3	7	7	17
	Normal	42	24	13	79
	High	5	2	0	7
Na+	Low	26	13	14	53
	Normal	24	20	6	50
Ca++	Low	50	36	13	99
	Normal	0	1	3	4
Chloride	Low	12	6	6	24
	Normal	36	25	13	74
	High	2	2	1	5

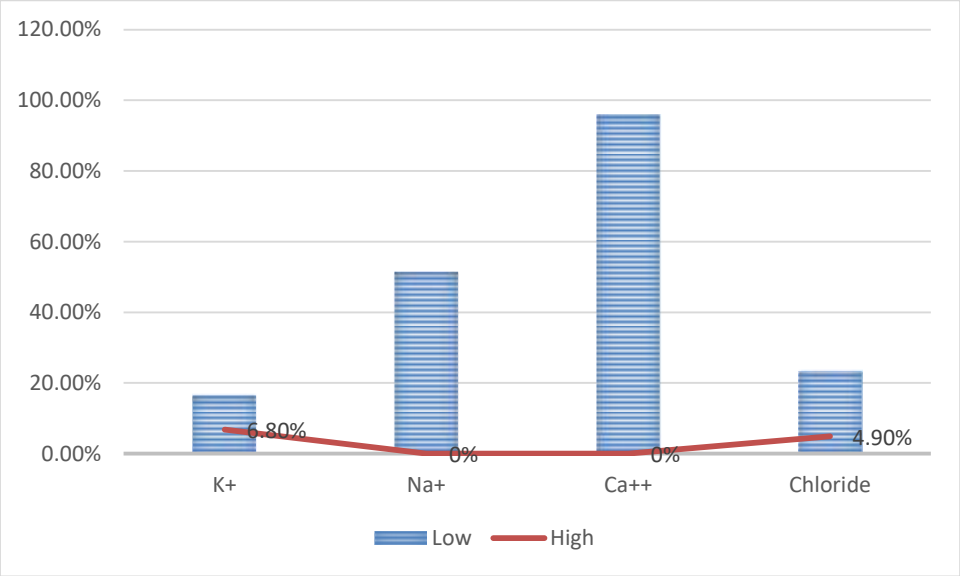

Fig 4: Description of the study population by GFR and K+, Na+, Ca++, and Chloride markers

DISCUSSION

The main goal of this cross-sectional study was to obtain genetic and biochemical data that can be used to improve health care in the future. CKD or renal failure in the general Saudi population is noticeably high, since there is a close homology within Saudi population in different areas. The findings of the present study show predominance of male sex rather than female. Although, some studies have reported such findings [7], other studies from the same region have reported inverse results [8, 9]. These discrepancies may be attributed to the type of study and sample size as they were greatly varies.

However, most of the study population was with severe renal impairment or renal failure, therefore, all of the biochemical markers were expected to be high. What is interesting is the variable levels of uric acid, particularly the high percentage of patients with low levels. Some studies have shown the links between hyperuricemia and CKD; though, the threshold of serum uric acid (SUA) for deterioration of kidney function and the association between SUA and kidney injury by baseline kidney function remains uncertain [10]. Although high uric acid was associated with reduced initial GFR, it was not an independent factor for the level of renal function impairment [11]. However, hypouricemia might be due to drugs or toxic agents [12], sometimes it is due to diet [13] or genetics [14].

Regarding minerals, K+ was low in 16.5% of the patients. These patients might be under dialysis. Post-dialysis hypokalemia can be a dangerous difficulty in patients who are already in total body potassium insufficiency [15]. Nevertheless, hyperkalemia may follow advanced stages of CKD. The failure of K+ renal excretion in end-stage renal disease causes K+ retention, and dangerous hyperkalemia develops;

subsequently K+ removal by dialysis is compulsory [16].

In this study hyponatremia was established in 51.5% of the cases. However, Patients with CKD can be affected by hyponatremia or hypernatremia, because of the high prevalence of comorbidities that can reduce the capability of the deteriorating kidneys to maintain an intact water homeostasis. Some studies have suggested that the incidence and prevalence of dysnatremias, particularly those of hyponatremia, are extensive in patients with non-dialysis-dependent CKD. Hyponatremia seems to affect outcomes similarly in patients with different stages of CKD, but hypernatremia appears to be correlated with simple consequences in those with more advanced stages of CKD [17].

In the present study a significant hypocalcemia was found. Calcium balance in CKD is poorly understood as hypocalcemia is a stimulus for secondary hyperparathyroidism and subsequent bone loss where as hypercalcemia stimulates extra-osseous calcifications [18]. Although, some studies have shown that normal calcium values are maintained up to very late stages of CKD [19, 20], but calcium balance in CKD is poorly understood.

Serum Chloride was also found to be low in a number of patients in the present study. Chloride administration was found to be hurtful to the kidney in critically ill patients. Conversely the link between plasma chloride concentration and renal function has poorly studied [21].Furthermore, a number of studies show neutral influence of chloride-restrictive line in protecting renal function [22, 23]. Notably, these studies are implemented in patients with contrast-induced nephropathy (CIN). It is likely that the protective effect of chloride-restrictive fluid is not universal and can only be present in critically ill patients.

For genetic analysis, we investigate the presence of Uromodulin (Tamm–Horsfall protein) mutation, since, it is the most abundant protein excreted in the urine under physiological conditions. Mutations in the gene encoding uromodulin lead to a progressive tubulo-interstitial damage, impaired urinary concentrating ability, hyperuricemia, renal cysts, and progressive renal failure [24]. However, Relatives with Uromodulin mutation have been reported from the several countries [25, 26], but not from KSA.

However, this study has several limitations including its cross sectional setting, randomization in selection of the study subjects and inclusion of those with severe renal impairment.

CONCLUSION

End stage of chronic kidney disease is prevalent in Northern KSA. Patients with CKD or renal failure have a diverse biochemical values which necessitate the urgent need for implantation of health strategies that can assist in the control of the disease and management of patients with disease. Further genetic investigations are required to explore the full image of uromodulin gene.

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REFERENCES

1. Qiu-Li Zhang, Dietrich Rothenbacher; Prevalence of chronic kidney disease in population-based studies: Systematic review. BMC Public Health 2008; 8:117.
2. Astor BC, Muntner P, Levin A, Eustace JA, Coresh J; Association of kidney functions with anemia: the Third National Health and Nutrition Examination Survey (1988–1994). Arch Intern Med 2002; 162(12): 1401-1408.
3. Pitts TO, Piraino BH, Mitro R, Chen TAIC, Segre GV, Greenberg A *et al.;* Hyper para thyroidism and 1, 25-dihydroxy vitamin D deficiency in mild, moderate, and severe renal failure. J Clin Endo crinol Metab 1988; 67(5): 876.
4. Locatelli F, Vecchio LD, Pozzoni P; The importance of early detection of chronic kidney disease. Nephrol Dial Transplant 2002; 17(Suppl 11): 2-7.
5. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am. J. Kidney Dis.2002; 39(2 Supple 1): S1–266.
6. Murphree DD, Thelen SM; Chronic Kidney Disease in Primary Care. J. Am. Board Fam. Med. 2010; 23(4):542-550.
7. Ahmed HG, Ginawi IA, Al-hazimi AM; Prevalence Estimates of Chronic Kidney Disease in Hail Region, KSA: in a Comprehensive Survey. International Journal of Science and Research, 2014; 3(7): 252-56.
8. Ginawi IA, Elasbali AM, Ahmed HG, Ashankyty IM, Altamimi T, Alhasan S, *et al.;* Population screening for chronic kidney disease and its associated risk factors: a survey in Hail region, KSA. J. Public Health Epidemiol.2013; 5(7): 285-290.
9. Ginawi IA, Ahmed HG, Ashankyty IM; Survey For Potential Risk Factors For Survey For Potential Risk Factors For Survey For Potential Risk Factors

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10. Toyama T, Furuichi K, Shimizu M, Hara A, Iwata Y, Sakai N *et al.;* Relationship between Serum Uric Acid Levels and Chronic Kidney Disease in a Japanese Cohort with Normal or Mildly Reduced Kidney Function. PLoS One,2015; 10(9): e0137449.
11. Miyeun Han, Hayne Cho Park, Hyunsuk Kim, Jo HA, Huh H, Jang JY *et al.;* Hyper uricemia and deterioration of renal function in autosomal dominant polycystic kidney disease. BMC Nephrol, 2014; 15(1): 63.
12. Ramsdell CM, Kelley WN; The clinical significance of hypouricemia. Annals of internal medicine, 1973; 78 (2): 239–42.
13. Szeto YT, Kwok TC, Benzie IF; Effects of a long-term vegetarian diet on biomarkers of antioxidant status and cardiovascular disease risk. Nutrition, 2004; 20 (10): 863–6.
14. Ichida K, Hosoyamada M, Kamatani N, Kamitsuji S, Hisatome I, Shibasaki T *et al.;* Age and origin of the G774A mutation in SLC22A12 causing renal hypouricemia in Japanese. Clin. Genet, 2008; 74 (3): 243–51.
15. Wiegand CF, Davin TD, Raij L, Kjellstrand CM; Severe hypokalemia induced by hemodialysis. Arch Intern Med, 1981; 141: 167-70.
16. Redaelli B, Bonoldi G, Di Filippo G, Vigano MR, Malnati A; Behavior of potassium removal in different dialytic schedules. Nephrol Dial Transplant,1998; 13(6): 35–38.
17. Kovesdy CP; Significance of hypo- and hypernatremia in chronic kidney disease. Nephrol. Dial. Transplant. 2012; 27 (3): 891-898.
18. Spiegel DM, Brady K; Calcium balance in normal individuals and in patients with chronic kidney disease on low- and high-calcium diets. Kidney International, 2012; 81: 1116–1122.
19. Levin A, Bakris GL, Molitch M, Smulders M, Tian J, Williams LA *et al.;* Prevalence of abnormal serum vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: results of the study to evaluate early kidney disease. Kidney Int, 2006; 71(1): 31–38.
20. Craver L, Marco MP, Martinez I, Rue M, Borràs M, Martín ML *et al.;* Mineral metabolism parameters throughout chronic kidney disease stages 1–5: achievement of K/DOQI target ranges. Nephrol Dial Transplant, 2007; 22(4): 1171–1176.
21. Zhang Z, Xu X, Fan H, Li D, Deng H; Higher serum chloride concentrations are associated with acute kidney injury in unselected critically ill patients. BMC Nephrology, 2013: 14: 235.
22. Klima T, Christ A, Marana I, Kalbermatter S, Uthoff H, Burri E *et al.;* Sodium chloride vs. sodium bicarbonate for the prevention of contrast medium-induced nephropathy: a randomized controlled trial. Eur Heart J 2012; 33(16): 2071-2079.
23. Maioli M, Toso A, Leoncini M, Gallopin M, Tedeschi D, Micheletti C, *et al.;* Sodium bicarbonate versus saline for the prevention of contrast-induced nephropathy in patients with renal dysfunction undergoing coronary angiography or intervention. J Am Coll Cardiol 2008; 52(8): 599-604.
24. Luca Rampoldi, Francesco Scolari, Antonio Amoroso, GianMarcoGhiggeri, Olivier Devuyst; The rediscovery of uromodulin (Tamm–Horsfall protein): from tubulo interstitial nephropathy to chronic kidney disease. *Kidney International 2011;* 80: 338-347.
25. Bollee G, Dahan K, Flamant M, Moriniere V, Pawtowski A, Heidet L et al.; Phenotype and outcome in hereditary tubulo interstitial nephritis secondary to UMOD mutations. Clin J Am Soc Nephrol. 2011; 6: 2429–2438.
26. Jennings P, Aydin S, Kotanko P, Lechner J, Lhotta K, Williams S et al.; Membrane targeting and secretion of mutant uromodulin in familial juvenile hyperuricemic nephropathy. J Am Soc Nephrol. 2007; 18: 264–273.