Biochemistry Section

A Comparative Study of Serum Uric Acid and Serum Magnesium Level in Diagnosed Cases of Various Renal Disorders

POLINA BORUAH¹, ARUP JYOTI BARUAH², ALICE ABRAHAM RURAM³, RANENDRA HAJONG⁴, CHANDAN KUMAR NATH⁵, BHUPEN BARMAN⁶

ABSTRACT

Introduction: Estimation of serum uric acid and magnesium along with other sensitive markers of renal function (serum creatinine and urea) are very effective to determine extent of renal impairment.

Aim: To compare the serum uric acid and magnesium level between controls and patients with various renal diseases and also to evaluate any correlation of these two parameters with severity of impairment (creatinine and urea).

Materials and Methods: Serum uric acid and magnesium estimation in 20 controls and 50 cases (28 males and 22 females; age 14-64 years) with various renal diseases (five cases of acute glomerulonephritis, 10 cases of acute renal failure, eight cases of acute pyelonephritis and 27 cases of chronic renal failure)

were done during a period of one year in North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences (NEIGRIHMS), Shillong, India.

Results: The serum magnesium and uric acid in control group were found within normal range with no significant variations observed in different age and sex. Both the parameters were found to be raised above their standard normal value in all 50 cases and also the parameters in the study showed positive correlation with serum creatinine and urea, so result of this study was significant (p-value <0.001).

Conclusion: Estimation of serum uric acid and magnesium are sensitive for the establishment of diagnostic and prognostic aspect in various renal diseases.

Keywords: Acute glomerulonephritis, Acute pyelonephritis, Acute renal failure, Chronic renal failure, Creatinine, Glomerular filtration rate, Urea

INTRODUCTION

The kidney performs several types of important vital functions of our body due to its complex morphological structure. It is the major organ responsible for the excretory function, regulation of body fluid volume (both extracellular and intracellular fluid) and composition (by the maintaining an appropriate balance of the concentration of body fluid electrolytes and acid-base) and secretion of a variety of hormones and autocoids. Studies of the renal diseases are facilitated by dividing them on the basis of involvement of four basic morphologic components of kidney e.g., renal glomerular diseases, renal tubular diseases, renal interstitial diseases, and renal vascular diseases. Early manifestations of renal diseases for each of the individual morphologic components tend to be a distinctive in character. Furthermore, some components appear to be more vulnerable to specific forms of injury; for example, glomerular diseases are often immunologically mediated [1], whereas tubular and interstitial disorders are more likely to be caused by toxic or infectious agents [2,3]. Nevertheless, some disorders affect more than one structure.

As the renal handling of magnesium and uric acid goes through various phases, so any impairment of renal function leads to derangement of both the parameters beyond its normal range. Renal handling of uric acid in human includes: (i) glomerular filtration; (ii) tubular reabsorption; (iii) secretion; and (iv) post-secretory reabsorption [4,5]; renal handling of magnesium via: (i) glomerular filtration; and (ii) tubular reabsorption [6,7]. Hence, serum uric acid and serum magnesium are very sensitive parameters for the assessment of severity of impairment of renal function along with other sensitive markers of kidney (serum creatinine and urea).

The present study aimed to compare the serum uric acid and magnesium level between controls and cases with various renal diseases and to compare the extent of deviation of serum levels of both parameters from the biological reference values along with severity of deterioration renal functions among these cases.

MATERIALS AND METHODS

This cross-sectional study was conducted at the Department of Biochemistry in North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences (NEIGRIHMS) for one year (from June 2012 to May 2013) after obtaining Ethical Clearance from the Institute (letter number NEIGR/IEC/2013/29).

Inclusion Criteria

Fifty diagnosed kidney disease cases were taken for this study. Various renal diseases in this study were Acute Glomerulonephritis (AGN)=five cases, Acute Pyelonephritis (APN)=eight cases, Acute Renal Failure (ARF)=10 cases and Chronic Renal Failure (CRF)=27 cases. Twenty consenting healthy individuals (13 male and 7 female; Age range 18-43 years) with normal renal function were taken as a control group and their serum magnesium and uric acid levels were estimated. Individuals of control groups were healthy volunteers of hospital staff nurses, laboratory technicians and hospital office staff.

Sample and control size was calculated by sample size calculating formula for comparison quantitative data between two groups for cross-sectional study. Global prevalence of chronic kidney diseases was 17.2% and study shows yearly increase of incidence 11% from 1992 to 2001 [8,9] α was <0.05 (Confidence Interval).

Exclusion Criteria

Patients who were receiving any type of hormonal replacement therapy, pregnant women and patients suffering from jaundice were not included in this study.

Specimen Collection and Preparation

Four millilitre blood was collected in vacutainer, allowed to clot completely then centrifuged at the rate of 1000 rpm for 10 minutes at 20°C. The supernatant serum was removed for analysis. Serum must be free from haemolysis. Serum magnesium, uric acid, creatinine and urea levels were estimated by using xylidyl blue, uricase, alkaline picrate and urease methods respectively in fully automated analyser Beckman- coulter AU2700. An amount of 450 μ L of serum was required for estimation. Residual fibrin and cellular matter was removed prior to analysis.

Prior to the estimation of biochemical parameters, instrument (AU-2700) was accurately calibrated and two levels of internal quality controls from Biorad were estimated for each parameter. Two levels of internal quality controls were accurate according to Levey-Jenning chart and did not violate Westgard rule. External quality control levels reports from CMC Vellore were accurate for the biochemical parameters [10].

STATISTICAL ANALYSIS

All the statistical analysis and level of significance were evaluated with unpaired t-test by using Microsoft Excel Office 365 in this study.

RESULTS

The results of mean values along with (±SD and p-value) of serum magnesium and serum uric acid in control group and various types of renal diseases are shown in [Table/Fig-1].

Mean of the Serum Magnesium levels						
Control group	50 Cases of various renal diseases	CRF	ARF	AGN	APN	
1.99±0.08	3.39±0.80	3.8±0.53 p<.001	3.57±0.49 p<.001	2.84±0.13 p<.01	2.06±0.19 p<.01	
Mean of the Serum Uric acid levels						
Control group	50 Cases of various renal diseases	CRF	ARF	AGN	APN	
4.65±0.27	7.67±1.02	8.08±0.82 p<.001	7.83±0.97 p<.01	7.40±0.57 p<.01	6.25±0.51 p<.01	
[Table/Fig-1]: Mean and SD values of serum magnesium and uric acid in control group and various types of renal diseases.						

Mean±SD values of serum magnesium in control group, CRF, ARF, AGN, APN were 1.99±0.08, 3.8±0.53, 3.57±0.49, 2.84±0.13, 2.06±0.19, respectively. Mean±SD values of serum uric acid in control group, CRF, ARF, AGN, APN were 4.65±0.27, 8.08±0.82, 7.83±0.97, 7.40±0.57, 6.25±0.51 respectively. Mean values of both serum magnesium and serum uric acid were increased in various types of renal diseases than that in control group.

The biological reference values are: Serum magnesium 1.9-2.7 mg/dL, Serum uric acid 3.4-7.0 mg/dL (Male) and 2.4-6 mg/dL (Female), Serum Creatinine 0.6-1.5 mg/dL (Male) and 0.5-1.2 mg/dL (Female), Serum Urea 20-40 mg/dL [11].

The values of Correlation coefficients of serum creatinine with serum magnesium and uric acid in various types of renal diseases are shown in [Table/Fig-2]. Correlation co-efficient between serum creatinine and serum magnesium in CRF, ARF, AGN, APN are 0.92, 0.48, 0.97 and 0.60 respectively.

Correlation coefficient between serum creatinine and serum uric acid in CRF, ARF, AGN, APN are 0.70, 0.61, 0.83, 0.73 respectively.

DISCUSSION

The critical factor responsible for the elevation of serum uric acid and serum magnesium level is the degree of reduction of filtration rate of the kidney [12,13]. Though in the present study, relation between GFR and two estimated parameters (serum uric acid and

Renal diseases (cases)	Correlation coefficient between serum creatinine and serummagnesium	Correlation coefficient between serum creatinine and serumuric acid		
CRF	0.92	0.70		
ARF	0.48	0.61		
AGN	0.97	0.83		
APN	0.60	0.73		
[Table/Fig-2]: Values of correlation coefficients serum creatinine with serum magnesium and uric acid in various types of renal diseases.				

serum magnesium) was not demonstrated, probably in various cases, the renal excretory capacity was greatly reduced due to decreased filtration as evident by considerable elevation of serum creatinine and blood urea level. The elevation of serum creatinine and blood urea level further supports the positive correlation of both biochemical markers (uric acid and magnesium) with deterioration of excretory function of kidney.

Hyperuricaemia occurs as a result of deterioration of excretory function of kidney and this in its turn causes further deterioration of renal function. The possible effect of hyperuricaemia on the deterioration of renal function experimented on Remnant Kidney (RK) in animal studies. In experimental animal (e.g., rat) hyperuricaemia was induced by the uricase inhibitor, Oxonic Acid (OA), results in hypertension, intrarenal vascular disease and renal injury. Increased uric acid in serum causes increased renal renin and Cycloxygenase-2 (COX-2) expression, the latter especially in preglomerular arterial vessels. COX-2 increased the synthesis of thromboxane $A_2(T_xA_2)$, T_xA_2 causes proliferation of smooth muscle cells of glomerular arterioles and thereby renal vasoconstriction which results in decreased glomerular filtration and deterioration of renal function [14-16].

Chronic Renal Failure (CRF)

In this study, serum uric acid concentration in all the 27 cases of CRF showed significant elevation.

The mean value of serum uric acid level was higher than the mean value of control. Identical results were also observed by some previous workers [17-20].

In this group, the mean value of serum magnesium was significantly elevated than the mean value of the control group. Similar results were also observed by some previous workers [21-23].

Acute Renal Failure (ARF)

All the 10 cases of acute renal failure in the oliguric phase showed significant elevation of serum uric acid and serum magnesium level than in the control group. The mean values of both of the parameter are also increased than the control group. Similar results were also observed by previous workers [24-26].

Acute Glomerulo-Nephritis (AGN)

In five patients with acute glomerulonephritis, the mean values of serum uric acid are higher than the mean value obtained in control group. Similar findings of high serum uric acid in patients with acute glomerulonephritis had been reported by other workers [27,28]. The mean values of serum magnesium level in these patients are higher than the value obtained in control group. In this group highest correlations are seen for both of parameters along with serum creatinine levels.

Acute Pyelonephritis (APN)

The mean values of serum uric acid were elevated than the mean value of control group. This could be accounted for by the possibility that production and excretion of the uric acid in these cases were greatly disturbed resulting in retention of uric acid in this group of cases [29]. The mean values of serum magnesium level in these patients somewhat higher than the mean value obtained in control group.

LIMITATION

The major limitation found during the study was inability to estimate GFR along with estimation of serum magnesium and uric acid due to lack of assessing facilities of the instrument. As the GFR is a very strong and sensitive biochemical markers of kidney function test which leaves scope for further studies on this topic along with GFR estimation.

CONCLUSION

Estimation of serum uric acid and magnesium are sensitive tools for the assessment of renal function. In this study, serum uric acid and serum magnesium levels were increased along with the increased serum levels of creatinine and urea in various renal diseases compared to control group, which is suggestive of reduced renal excretory function. The present authors can estimate the severity of deterioration of kidney function in various renal diseases by measuring both of the parameters because both of them showing positive correlations along with serum creatinine levels. However, in future, more studies are required for both of the parameters in various renal diseases along with the measurement of GFR to establish the sensitivity of the parameters in various renal diseases.

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REFERENCES

- William GC. Basic and translational concepts of immune-mediated glomerular diseases. J Am Soc Nephrol. 2012;23(3):381-99.
- [2] Marian G, Francisco R, Juan ML. Increased prevalence of acute tubulointerstitial nephritis. Nephrol Dial Transplant. 2013;28(1):112-15.
- [3] Baker R, Pusey C. The changing profile of acute tubulointerstitial nephritis. Nephrol Dial Transplant. 2004;19(1):8-11.
- [4] Ion AB, Orson WM. Renal transport of uric acid: evolving concepts and uncertainties. Adv Chronic Kidney Dis. 2012;19(6):358-71.
- [5] Cosimo MB, Gabriele P, Damiano C. Tubular handling of uric acid and factors influencing its renal excretion: a short review. Eur Med J Nephrol. 2016;4(1):92-97.
- [6] Quamme GA, De RC. Epithelial magnesium transport and regulation by the kidney. Front Biosci. 2000;5:D694-711.
- [7] Quamme GA, Dirks JH. The physiology of renal magnesium handling. Ren Physiol. 1986;9(5):257-69.
- [8] Ajay KS, Youssef MK, Bharati VM. Epidemiology and risk factors of chronic kidney disease in India- results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. BMC Nephrol. 2013;14:114.

- [9] Cerda J, Lameire N, Eggers P. Epidemiology of acute kidney injury. Clin J Am Soc Nephrol. 2008;3(3):881-86.
- [10] Greg Cooper, CLS, MHA Manager of Clinical Standards and Practices. Basiclessons in laboratory quality control. California, United States: Bio-RadLaboratories, Inc. Quality System Division; 2008. Available from: http://www. bio-rad.com/qualitycontrol U.S. [Accessed 23rd December 2017].
- [11] William LR, Gwendolyn AM, Carl AB, David EB. Reference Information for the Clinical Laboratory. In: Carl A. Burtis, Edward R. Ashwood, David E. (eds.) Tietz Fundamentals of Clinical Chemistry; sixth ed. Published by Elsevier: Reed Elsevier India; 2008. ch 45; Pp.837-862.
- [12] Randall RE, Cohen MD, Spray CC. Hypermagnesemia in renal failure: etiology and toxic maifestations. Ann Intern Med. 1964;61:8873.
- [13] De Oliveira EP, Burini RC. High plasma uric acid concentration: causes and consequences. Diabetology and Metabolic Syndrome. 2012;4:12.
- [14] Duk HK, Takahiko N, Lili F. A role for uric acid in the progression of renal disease. J Am SocNephrol. 2002;13(12):2888-97.
- [15] Hernandez J, Astudillo H, Escalante B. Angiotensin II stimulates cyclooxygenase-2 mRNA expression in renal tissue from rats with renal failure. Am J Physiol Renal Physiol. 2002;282(4):F592-F598.
- [16] Mazzali M, Kanellis J, Han L. Hyperuricaemia induces a primary arteriolopathy in rats by a blood pressure independent mechanism. Am J Physiol Renal Physiol. 2002;282(6):F991-97.
- [17] Short RA, Tuttle KR. Clinical evidence for the influence of uric acid on hypertension, cardiovascular disease, and kidney disease: a statistical modelling perspective. Semin Nephrol. 2005;25(1):25-31.
- [18] Kang DH, Chen W. Uric acid and chronic kidney disease: new understanding of an old problem. Semin Nephrol. 2011;31(5):447-52.
- [19] Mok Y, Lee SJ, Kim MS. Serum uric acid and chronic kidney disease: the Severance cohort study. Nephrol Dial Transplant. 2012;27(5):1831-35.
- [20] Rodenbach KE, Schneider MF, Furth SL. Hyperuricaemia and progression of CKD in children and adolescents: The Chronic Kidney Disease in Children (CKiD) cohort study. Am J Kidney Dis. 2015;66(6):984-92.
- [21] Tibor Fulop; Chief Editor: Vecihi Batuman. Hypermagnesemia. Available from: http://emedicine.medscape.com/article/246489 [Accessed 27th February 2017].
- [22] Sharma SK, Singh R, Patney NL. Serum magnesium levels in chronic renal failure. Clinical significance and correlation with sodium potassium and calcium. J Assoc Physicians India. 1990;38(8):569-71.
- [23] Avasthi G, Singh HP, Katyal JC. Copper, zinc, calcium and magnesium in chronic renal failure. J Assoc Physicians India. 1991;39(7):531-4.
- [24] Mark TF; Chief Editor: Vecihi Batuman. Uric Acid Nephropathy. Available from: http://emedicine.medscape.com/article/244255 [Accessed 27th February 2017].
- [25] Ahsan E, Wei M, Duk HK. Could uric acid have a role in acute renal failure? Clin J Am Soc Nephrol. 2007;2:16-21.
- [26] Amit N, Rakesh S, Pranay D. Study of serum magnesium level in acute kidney injury and chronic kidney disease and its clinical manifestations and correlation with other biochemical parameters. JEMDS. 2015;4(74):12928-33.
- [27] Moutoussis G, Klein G. Acute glomerulonephritis preceded by passage of uric acid calculus. The Lancet. 1978;312(8104):1376-77.
- [28] Kuniyoshi Y, Kamura A, Yasuda S. Post-streptococcal acute glomerulonephritis complicated by gouty arthritis: a case report. Pediatr Rheumatol Online J. 2015;13:24. Published online 2015 Jun 17th. Available from: doi: 10.1186/ s12969-015-0019-7 [Accessed 27th february2017].
- [29] Nickeleit V, Mihatsch MJ. Uric acid nephropathy and end-stage renal disease-Review of a non-disease. Nephrol Dial Transplant. 1997;12:1832-38.

PARTICULARS OF CONTRIBUTORS:

- 1. Lecturer, Department of Biochemistry, North Eastern Institute of Ayurveda and Homeopathy, Shillong, Meghalaya, India.
- 2. Associate Professor, Department of General Surgery, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India.
- 3. Associate Professor, Department of Biochemistry, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India.
- 4. Associate Professor, Department of General Surgery, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India.
- Assistant Professor, Department of Biochemistry, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India.
- Associate Professor, Department of General Surgery, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Arup Jyoti Baruah

Associate Professor, Department of General Surgery, Room No. 25, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Ma Wdiangdiang, East Khasihills, Shillong-793012, Meghalaya, India. E-mail: arupbaruah06@gmail.com

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