ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 10, Issue, 10, pp.74747-74750, October, 2018

DOI: https://doi.org/10.24941/ijcr.32884.10.2018

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

KIDNEY MORPHOLOGICAL CHANGESIN PATIENTS WITH ASYMPTOMATICHYPERURICEMIA AND CHRONIC KIDNEY DISEASE

***Kolarska, Y. and Deliyska, B.**

Nephrology Clinic, University Hospital "Queen Yoanna-ISUL" Medical University, Sofia, Bulgaria

ARTICLE INFO

Article History:
Received 29th July, 2018
Received in revised form
12th August, 2018
Accepted 07th September, 2018
Published online 31st October, 2018

Key Words:
Asymptomatic Hyperuricemia, морphological Changes, Chronic Kidney Disease, Proteinuria, Blood Pressure.

ABSTRACT

Background: The aim of the study is to take into account the relationship between asymptomatic hyperuricemia (a HU) and morphological changes in the kidneys. **Materials and Methods:** A retrospective analysis of kidney biopsy of 110 patients divided into two groups: with a HU (n = 62) and non- HU (n = 48).We analyzed each morphological change separately in the respective groups, then the data were compared between the two groups. A multifactorial analysis was performed between the degree of the morphological changes and proteinuria (PU), systolic blood pressure (SBP), and diastolic blood pressure (DBP), that are factors for non-immune progression of chronic kidney disease (CKD). **Results:** When comparing only the morphological changes between the two groups, no statistically significant difference was found. Patients with a HU and severe mesangial cells proliferation, the PU was higher - 4.31 +/- 4.6 g /24 h if compare with non-HU 2.64 +/- 2.28 g /24 h. The same dependence is reported in the presence of significant interstitial infiltrates and interstitial fibrosis, and the marked changes in extraglomerular vessels. Expression of tubular atrophy in a HU group is associated with higher SBP than the control group: 143.75 +/- 18.47 mmHg and 117.7 +/- 35.94 mmHg. **Conclusions:** Correlation was established in patients with a HUand pronounced interstitial fibrosis, and with changes in extraglomerular vessels. Patients with a HU and interstitial infiltrates had higher PU. The association of a HU with some morphological changes results with higher SBP, DBP, and PU that are factors relevant to the progression of CKD.

Copyright © 2018, Kolarska and Deliyska. *This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.*

***Citation: Kolarska, Y. and Deliyska, B.* 2018.** "Kidney morphological changesin patients with asymptomatichyperuricemia and chronic kidney disease", *International Journal of Current Research*, 10, (10), 74747-74750.

INTRODUCTION

The importance of asymptomatic hyperuricemia on the progression of chronic renal failure has only been studied since the last decade and has become a relatively new risk factor that has a bearing on many pathological conditions (Filiopoulos *et al*., 2012; Kang *et al*., 2005; Mazzali *et al*., 2002). In literature, there are extremely rare data about the elevated levels of serum uric acid (sUA) with morphological changes in immune and autoimmune nephropathies (Deliyska *et al*., 2009; Eun-Sun *et al*., 2013; Jinde, 2001). It is not entirely clear whether a HU further aggravates and enhances some histopathological changes in glomerulopathies. In this study, we have reported the relationship between a HU and the degree of morphological changes in the kidneys in immune and autoimmune nephropathies.

***Corresponding author:*Kolarska, Y.,**
Nephrology Clinic, University Hospital "Queen Yoanna-ISUL" Medical University, Sofia, Bulgaria.

MATERIALS AND METHODS

This study included 110 patients, hospitalized with renal biopsy at the Nephrology Clinic, University Hospital "Queen Joanna-ISUL". The patients were divided into 2 groups - 62 of them with a HU and 48 patients without elevated sUA levels. In order to take into account the influence of a HU on morphological changes, the histological changes in each group were separately analyzed. Subsequently, the data are between the two groups compared. Serum UA is by the enzyme colorimetric test determined. An increased sUA is for HU considered: in men over 420 μmol /l and in women over 340 μmol /l. The results of the laboratory tests are reported in SI units. In both groups were the following clinical and laboratory values recorded: age(years), duration of the kidney disease (months), duration of hypertension (months), SBP(mmHg), DBP(mmHg), PU(g/24h), plasma-creatinine (μmol/l), eGFR(ml/min/1,73m2) according to MDRD, serum albumin (g/l), cholesterol (mmol/l), triglyceride (mmol/l) and sUA (μmol/l). The CKD grades were according to KDIGO-2012 determined.

The morphological changes were reported semi-quantitative graded using a semi quantitative scale. Such were: mesangial cell proliferation, mesangial matrix enlargement, glomerulosclerosis, tubular atrophy, interstitial infiltrates, interstitial fibrosis, and changes in non-glomerular vessels. A semiquantitative scale was of 1 to 3+ used, 1+ lacking morphological change, 2 moderate and 3+ diffuse expression. With immunofluorescence staining semi quantifiable from 1- missing to 4+, the intensity and location of immune deposits were heavily accounted.The statistical analysis was with Microsoft Excel 2013 and SPSS Statistics 22.0 performed. For a level of significance in which the zero hypothesis was rejected, $p < 0.05$ was accepted.

RESULTS

Comparative analysis of the groups was performed, taking into account some clinical laboratory parameters such as age, renal disease, hypertension, SBP, DBP, plasma-creatinine, eGFR, PU, serum albumin, serum cholesterol, triglyceride, and serum UA. The mean age of the two groups is without significant difference or difference 42.46 +/- 16.12 g in patients with a HU and 47.35 +/- 13.87g in the control group ($p > 0.05$). Of all the pains in both groups, 67 (60.9%) are men and 43 (39.1%) are women. The limit of hypertension in the a HU group was 26.63 +/- 46.50 months, compared with the non- HU22.52 +/- 35.50 months ($p < 0.05$). Proteinuriain the a HU group was 3.75 +/- 3.64g /24h, and non- HU 3.00 +/- 3.77g /24h ($p > 0.05$). Triglycerides were slightly higher in patients with the group with a HU 2.02 +/-1.00 mmol /l compared to those non- HU 1.86 +/- 0.96 mmol /l. A statistically significant difference in sUA levels was observed, which was 321 +/- 67.53 μmol /l for the non-HU group and 474.24 +/- 84.22 μmol /l for the a HU group ($p < 0.001$) (Table 1).

There was no significant difference between the two groups in the extent of morphological changes in the renal biopsy. The most common finding in both groups was mesangial hypercellularity (MsH) and matrix accumulation without significant difference between them ($p > 0.05$).Patients with a HU were more likely to have tubular atrophy, interstitial fibrosis, and interstitial cell infiltrate and changes in non-glomerular vessels compared to the control group but with no statistically significant difference between the groups ($p>0.05$). There is no statistically significant difference in the type and intensity of immune deposits in the studied materials between the two groups. Data comparing with SBP, DBP, and PU in the a HU group compared with controls revealed that patients with pronounced mesangial cell proliferation and without a HU had a significantly lower PU of 2.64 ± 2.28 g /24h of the group with a HU and 4.31 +/- 4.60 g /24h (Table 2). Patients with a HU and moderately increased mesangial matrix were significantly higher in PU than the control group with the same change rate of 4.45 +/- 4.48 g / 24 h and 2.57 +/- 2.81 g / 24 h (Table 3).In moderate glomerulosclerosis lesions (GsL) in the a HU group, higher values of DBP or 91+/- 12.5 mmHg were observed relative to the control group with the same morphological change rate of 79.55 +/- 11.93 mmHg (Table 4).Patients with a HU have tubular atrophy (TA) had a higher SBP compared to the control group of 143.75 +/- 18.47 and 117.50 +/- 35.94 mmHg (Table 5). Patients with a HU and pronounced interstitial infiltrates (InInf) had a higher SBP than the control group of 148.33 +/- 20.65 mmHg and 136.82 +/- 25.52 mmHg respectively. Diastolic blood pressure values in a HU with pronounced interstitial infiltration were also higher - 91.67 +/- 91.67 mmHg relative to the control group, which were 82.73 +/- 11.04 mmHg. In moderate and pronounced interstitial infiltrates. Patients with a HUhad a higher PU, respectively, at moderate 4.51 +/- 4.4 g / 24 h and at a significant 3.11 +/- 2.93 g /24 h and in the non-HU group at moderate 2 , 46 +/- 2.53 g / 24 and significant 2.49 +/- 1.19 g /24 h.SBP is higher in patients with a HU and with interstitial fibrosis (InF) compared to the control group 156.15 +/- 19.81mmHg and 144.17 +/-32.04mmHg.Asymptomatic HU patients with moderate interstitial fibrosis were with higher PU than those without HU 2.99 +/- 2.95 g/24h, and 1.55 +/- 1.05 g/24h. Patients with a HU and with interstitial fibrosis also had a higher PU than controls - 5.32 +/- 5.24 g/24h respectively and 3.85 +/- 4.90 g/24h.Patients with a HU and pronounced changes in extra-cellular vessels had a higher SBP than the control group - 144.29 +/- 22.25mmHg and 133.57 +/- 29.54mmHg.Patients with elevated sUA levels with moderate and expressed vessel changes were significantly higher in PU compared to the control group, with moderate vascular changes of 3.06 +/- 2.76 g /24h and 2, 93 +/- 2.22 g /24h, and for significant variations respectively 2.44 +/- 2.12 g/24h and 1.90 +/- 1.12 g /24h.

DISCUSSION

In literary data analysis were, a relatively small number of publications associated with histomorphologic changes from the renal biopsy in a HU patients and with immune and autoimmune diseases, found. In patients with IgA-nephropathy, elevated sUA levels are an independent risk factor for CKD development and increased mortality (Bakan, 2015; Knoop, 2013; Ohno, 2011).Several publications related to clinical-pathological changes in HU patients analyze histological changes in patients with IgA nephropathy (Cheng, 2013; Cui *et al*., 2011; Shi *et al*., 2012). In one of these, the authors track the results in 171 patients, dividing them into three groups: normotensive and normouremic, normotensive and hyperuricemic and hypertensive and hyperuricemic. They find that patients with this nephropathy, who are also with elevated uric acid, have more severe clinical-pathological changes, and the presence of arterial hypertension increases them further (Lozada *et al*., 2005).In his study, Verzola D and collaborators in experimental conditions attempted to assess the importance of PK on tubular-interstitial changes in the kidney. They note that PC probably increases proximal tubule cell apoptosis with NADPH oxidase and URAT1 transport. The authors associate tubulointerstitial changes in HU with apoptosis (Verzola *et al*., 2004). The data from the present study did not account for a significant difference in the type and extent of histological changes in patients with and without HU. It was observed that the elevated level of sUA in combination with some morphological alterations was associated with higher PU compared to the control group of patients without HU. Data analysis also suggests an additional adverse effect of the combination of PU and HU on part of the morphological changes in the kidney tissue. We can assume that the combination of high-grade PU with a HU is associated with the development of significant interstitial fibrosis.In patients with a HU and interstitial infiltrates, SBP, DBP was reported to be higher than the control group. Tubular atrophy and interstitial fibrosis, as well as changes in the extracellular vessels a HU, are also combined with a higher SBP than the control group. Pathological histological alterations such as glomerulosclerosis and interstitial infiltrates are associated with a higher level of DBP in a HU group.

Table 1. Comparative analysis of groups without and with a HU on the quantitative indicators surveyed

Indicator	Non HU (n=48)		With a HU(n=62)		p
		SD		SD	
age (years)	42,46	16.12	47.35	13.87	0.090
Duration of kidney disease (months)	25.75	51.26	24.42	54.97	0.265
Limit of hypertension (months)	22.52	35.50	26.63	46.50	0.737
SBP (mmHg)	141.04	29.43	144.42	20.30	0.417
DBP (mmHg)	86.46	14.91	86.94	12.02	0.610
PU(g/24 h)	3.00	3,77	3.75	3.64	0.119
plasma-creatinine(µmol/l)	208.57	111.45	212.60	143,47	0.589
eGFR (ml/min/1,73m^2)	44.67	27.18	49.75	34.18	0.691
serum albumin (g/l)	34.94	8.73	35.69	8.89	0.657
serum cholesterol(mmol/l)	6.34	1.38	6,78	2,27	0.942
triglyceride (mmol/l)	1.86	0.96	2.02	1.00	0.456
sUA (µmol/l)	321.96	67.53	474.24	84.22	<0,001

Table 2. Comparative analysis of SBP, DBP, and PU by mesangial cell proliferation group with and non- HU

Indicator	MsHnon- HU	n	SD		MsHwith a HU	n	SD	
SBP (mmHg)	1+	15	133.33	28.95	1+	19	144.42	18.69
	2+	14	139.64	23.73	2+	19	148.42	24.33
	3+	19	148.16	33.13	3+	24	141.25	18.25
DBP (mmHg)	1+	15	83.33	14.47	1+	19	87.11	12.05
	2+	14	85.36	11.84	2+	19	87.89	13.16
	3+	19	89.74	17.20	3+	24	86.04	11.51
PU(g/24 h)	1+	15	2.65	4.42	1+	19	3.33	3.62
	2+	14	3.86	4.69	2+	19	3.47	2.03
	3+	19	2.64	2.28	3+	24	4.31	4.60

Table 3. Comparative analysis of SBP, DBP, and PU by mesangial matrix increment in groups withand non- HU

Indicator	M.matrixwith a HU	n		SD	M.matrixnon- HU	n		SD
SBP (mmHg)	1+	23	148.7	20.74	1+	20	140.5	26.30
	2+	33	142.24	21.06	2+	25	140.00	30.69
	3+	6	140.00	12.65	3+	3	153.33	47.26
DBP (mmHg)	1+	23	88.70	13.59	1+	20	85.00	13.57
	2+	33	86.21	11.32	2+	25	87.2	16.14
	3+	6	84.17	10.21	3+	3	90.00	17.32
PU(g/24 h)	1+	23	2.91	2.93	1+	20	3.59	4.90
	2+	33	4.45	4.08	2+	25	2.57	2.81
	3+	6	3.13	3.29	3+	3	2.60	2.16

Table 4. Comparative analysis of SBP, DBP, and PU according to glomerulosclerosis lesions in groups with and non- HU

Indicator	GsL with a HU	n		SD	GsL non- HU	n		SD
SBP (mmHg)	1+	29	148.76	19.76	1+	28	139.46	28.56
	2+	20	144	19.84	2+	11	130.45	29.36
	3+	13	135.38	20.66	3+	9	158.89	27.13
DBP (mmHg)	1+	29	85	11.10	1+	28	86.25	15.31
	2+	20	91	12.52	2+	11	79.55	11.93
	3+	13	85	12.58	3+	9	95.56	13.33
PU (g/24 h)	1+	29	4,3	4.27	1+	28	1.66	1.17
	2+	20	3,16	3.39	2+	11	4.89	5.20
	3+	13	3,43	2,34	3+	9	4,85	5,47

Table 5. Comparative analysis of SBP, DBP, and PU by tubular atrophy in the group with and without HU

Indicator	TAwith a HU	n		SD	TAnon- HU	n		SD
SBP	1+	27	147.56	20.49	1+	30	140.67	26.93
(mmHg)	2+	27	141.48	20.88	2+	14	148.57	31.34
	3+	8	143.75	18.47	3+	4	117.50	35.94
DBP (mmHg)	1+	27	87.78	12.27	1+	30	86.83	14.53
	2+	27	86.3	12.53	2+	14	88.93	14.70
	3+	8	86.25	10.61	3+	4	75.00	17.32
PU (g/24 h)	1+	27	5.06	4.58	1+	30	2.32	2.98
	2+	27	2.84	2.43	2+	14	4.09	4.79
	3+	8	2.44	2.04	3+	4	4.23	5.01

We can summarize that a HU does not have a significant self-importance in the type and severity of morphological changes of the kidney. Its combination with some histological changes manifested largely is associated with worsening clinical and laboratory signs such as hypertension and PU.It can be assumed that asymptomatic HU is an immune co-factor for the progression of in immune and autoimmune nephropathies CKD.

REFERENCES

Bakan A., Oral A, *et al*. 2015. Hyperuricemia is associated with progression of Ig A nephropathy. *Int. Urol. Nephrol.,* Apr; 47(4):673-8. .

Cheng GY and Liu DW. *et al*., 2013. Clinical and prognostic implications of serum uric acid levels on IgA nephropathy: a cohort study of 348 cases with a mean 5-year follow-up. *Clin. Nephrol.,* 80:40–6.

Cui MJ., Zhang BH. *et al*. 2011. The relationship between hyperuricaemia and clinic pathology of IgA nephropathy. Zhonghua Nei Ke Za Zhi.50:659–63.

Deliyska B., Vasilev V.*et al*. 2009.C3 Depositions in Proximal Tubular Epithelial Cells are Common in Minimal Change Disease and in IgM Nephropathy, BANTAO Journal., 7 (2): 10-13

Eun-Sun Ryu, Mi Jin Kim*et al*. 2013. Uric acid-induced phenotypic transition of renal tubular cells as a novel mechanism of chronic kidney disease, *Am J Physiol Renal Physiol*., 304: F471–F480.

Filiopoulos V., Hadjiyannakos D., Vlassopoulos, D. 2012. New insights into uric acid effects on the progression and prognosis of chronic kidney disease.*Ren Fail.,* 34(4):510-20.

Jinde K., Nikolic-Paterson DJ., Huang XR., Sakai H., Kurokawa K., Atkins RC., Lan HY. 2001. Tubular phenotypic change in progressive tubulo-interstitial fibrosis in human glomerulonephritis. *Am. J. Kidney.,* Dis38:761–769.

Kang DH.[1], Nakagawa, T. *et al*. 2005. Uricacid and chronic renal disease: possible implication of hyperuricemia on progression of renal disease, Semin *Nephrol.,* Jan; 25(1):43-9.

Knoop T., Vikse BE, *et al*. 2013. Bjørneklett R. Mortality in Patients with IgA Nephropathy. *Am. J. Kidney Dis,*.

LozadaL., TapiaE, SantamariaJ*et al*. 2005. Mild hyperuricemia induces vasoconstriction and maintains мglomerular hypertension in normal and remnant kidney rats. Kidney Internation. 67:237-47.

Mazzali M., Kanellis J, *et al*. 2002. Hyperuricemia induces a primary arteriolopathy in rats by a blood pressure-independent mechanism. *Am. J. Physiol Renal Physiol*., 282: F991–F997,

Ohno I. 2011. Relationship between hyperuricemia and chronic kidney disease. Nucleosides Nucleotides Nucleic Acids. 30:1039–44.

Rastaldi, M.P. Ferrario, F. *et al*. 2002. Epithelial-mesenchymaltransitionoftubularepithelialcellsinhumanrenalbiopsies. *Kidney Int,* 146, 62: 137

Shi Y., Chen W., Jalal D., Li Z., Chen W., Mao H. *et al*. 2012. Clinical outcome of hyperuricemia in IgA nephropathy: a retrospective cohort study and randomized controlled trial. *Kidney Blood Press Res.,* 35:153–60.

Verzola D.[1], Bertolotto MB. *et al*. 2004. Oxidative stress mediates apoptotic changes induced by hyperglycemia in human tubular kidney cells, *J. Am. Soc. Nephrol.,* Jan;15 Suppl 1:S85-7.

****