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The Relationship between Serum Uric Acid Level and Pulmonary Artery Hypertension in Patients with Chronic Renal Failure

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ABSTRACT

Background and aim: Uric Acid is the final production of purine metabolism. The serum concentration of this substance is related to purine metabolism and renal clearance. Pulmonary hypertension (PH) in patients with CKD may be induced or aggravated by left ventricular (LV) disorders. The presence of risk factors typical to CKD is including volume overload, an arteriovenous fistula, sleep-disordered breathing. Exposure to dialysis membranes, endothelial dysfunction, vascular calcification and stiffening, and severe anemia.

Materials and methods: In this study relation between Uric Acid levels and PH in 70 patients with non-dialysis renal failure (41 females, 29 males) with a mean age of 61.71±12.44 years were assessed. The required information is extracted from the patients' records based on the questionnaire. Finally, the results are analyzed according to the SPSS program.

Results: PH was defined as a PASP ⩾ 35 mmHg by echocardiography. 36 CKD patients had PH (51.4%). Average Uric Acid levels in patients with PH were significantly higher than healthy controls ($p = 0.003$). For 1mmHg increase Uric Acid, 0.94 mmHg in pulmonary artery pressure level will increase. There was no significant difference between patients with PH and patients without PH according to age, gender, BMI, MAP, GFR, EF, RV size & function, LV diastolic dysfunction, SMRV, and TAPSE.

Conclusion: Control of high Uric Acid levels and the treatment of risk factors of PH for prevention PH seems reasonable.

1. Introduction

Uric acid is the final product of purine metabolism. Its serum concentrations are related to the amount of purine metabolism and renal clearance. Therefore, significant levels of Uric Acid accumulate in patients with chronic/ end-stage renal disease.[1] Uric acid increases in hypoxia, such as chronic heart failure,[2] congenital cyanotic heart disease[3], and obstructive pulmonary disease.[4] The average pulmonary arterial pressure, measured by intrusive (catheterization) methods, is 25 mmHg. While usually with non-invasive echocardiography, the pulmonary artery's systolic pressure is measured, assuming a RA pressure of 3 to 5 mmHg, the average systolic pressure of the pulmonary artery is 35 to 36 mmHg (with a maximum TR Gradient = 2.8 - 2.9).[5] Pulmonary arterial hypertension in patients with chronic renal failure can be due to left ventricular dysfunction due to complications of chronic kidney disease such as volume overload, arterial-venous fistula in the form of dialysis,[6] contact with dialysis membranes,[7] sleep disturbance and respiration,[8] endothelial dysfunction,[9] and calcification. The rigidity of the vessels and severe anemia[10] may be developed or exacerbate de. Despite the different causes of PHTN, there are similar clinical and physiopathological manifestations.[11] Few studies have been conducted on the prevalence of pulmonary arterial hypertension and its association with Uric Acid levels in non-dialysis patients with chronic renal failure. Considering that the most common cause of mortality in patients with chronic renal failure is cardiovascular causes, it is necessary to recognize the related factors. Also, the prevention of pulmonary arterial hypertension in patients with chronic renal failure is important because, if it occurs, mortality increase[11] even if the patients undergo kidney transplantation. In this study, the serum levels of Uric Acid in patients with chronic non-dialysis kidneys are studied, and their association with

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pulmonary arterial hypertension will be investigated. Given the fact that many patients with chronic renal failure are candidates for renal transplantation, with timely treatment, it can prevent the onset of pulmonary arterial hypertension, which can increase mortality even when a kidney transplant is performed. In this study, the serum levels of uric acid in patients with chronic non-dialysis kidney are studied, and its association with pulmonary arterial hypertension will be investigated. Given the fact that many patients with chronic renal failure are candidates for renal transplantation, with timely treatment, it can prevent the onset of pulmonary arterial hypertension, which can increase mortality even when a kidney transplant is performed.

2. Materials and methods

This study is a cross-sectional study in which 70 non-dialysis patients with chronic renal failure referring to Imam Khomeini Hospital in 2016. according to inclusion criteria (including all patients with chronic renal failure (GFR <60), non-diabetic patients dialysis referred to Imam Khomeini Hospital this year), and exit criteria include chronic lung disease (COPD, ILD), pulmonary thromboembolism, obstructive sleep apnea, systemic disorders. Connective tissue disorders such as sarcoidosis and systemic scleroderma and vasculitis, congenital heart disease. The required information is extracted from the patients' records based on the questionnaire. Finally, the results are analyzed according to the SPSS program. The goals are summarized based on the questionnaire and finally analyzed using the SPSS software. The calculation of the data is based on the following formula.

(r-value is calculated according to Chun-Yan Zhang's article [15])

$n= [(Z\alpha+Z\beta)/C] 2$

$Cr=0.5 \times Ln [(1+r)/ (1-r)]$ $r=0.387$ $\alpha=0.05$ $\beta=0.1$

$Z1-\frac{\alpha}{2}=1/96$, $Z1-\beta=1/28$

$n= 67 \sim 70$

Because all patient information is from the case file and without mentioning to their name, and after receiving the Ethics Committee of Theses' approval, it does not cause any ethical issues. In some patients, the absence of TR leads to the fact that PAP cannot be measured, removed from the list, to eliminate the bias of these patients. Specifications such as Uric Acid, creatinine, age, sex, and allopurinol have been extracted from the patient's file.

3. Results

In this study, 70 patients with chronic renal failure with mean (SD) age (71/61) year (12.44), 41(58.5%) women, and 29(41.4%) males were examined. Thirty-six of them (51.4%) had PHTN. The demographic and clinical characteristics of the subjects based on pulmonary arterial pressure are shown. The difference between age, sex ratio, and BMI was not statistically significant in normal and PHTN groups (P> 0.05). The mean of Uric Acid level in subjects with PHTN was higher than normal subjects, and the difference was statistically significant (P= 0.003). No significant correlation was found between the levels of renal insufficiency (GFR) and PHTN. Also, the observed difference between creatinine levels in the two groups was not statistically significant (P> 0.05). The difference between SBP, DBP, and MAP levels between the two groups was not statistically significant (P> 0.05). For an increase of 1 milligram per 1 mg / dl of uric acid, 94.9 millimeters .94mmHg (about 95% confidence interval: 0.17- 1.7) it is increased to the surface Pulmonary artery pressure (p = 0.018). The differences observed between the two groups of normal and those with PHTN were statistically significant for the causes of CKD (P-value = 0.05), so that 13 (36.1%) of people with PHTN, with HTN and DM, were co-administered. In contrast, those in the group with normal pulmonary arterial pressure were found only in 2 (5.9%) patients. No significant correlation was found between EF, Rv Size, Rv Function, LV diastolic dysfunction, TAPSE, SMRV, and PHTN.

4. Discussion

Hypertension is defined as an increase in pulmonary arterial pressure and increased vascular resistance, with PAP> 25 mmHg at rest and PAP> 30 mmHg in active mode. with pulmonary pressure> 15 mmHg performed by right cardiac catheterization, and regardless of its cause, it is accompanied by increased morbidity and mortality.[17] Despite the different causes of PHTN, there are similar clinical and physiopathological manifestations.[11] EPA is a non-invasive method, and echocardiography plays a vital role in the diagnosis, prognosis, and follow-up of patients.[5] PAP measurements by echocardiography are based on TR.[18] The prevalence of PHTN in patients with pre-dialysis stage 5 CKD,[11,19] 9.39%, in hemodialysis was 18.8-8.88, peritoneal dialysis was 0.42%.[20] Few epidemiological studies are available on the incidence of PHTN in lower CKD stages.[18] In this study, PAP ≥ 35 mmHg was the basis for the diagnosis of PHTN. In our study, we examined 36 patients with PAP ≥ 35 mmHg (51.4%). The main finding of this study is the existence of a significant relationship between Uric Acid levels and the occurrence of PHTN. This finding was consistent with the Nagaya study[12] and was inconsistent with Bendayan's[13] study. In a study by Nagaya et al. (1999) in Japan, which was done on 90 patients with primary pulmonary hypertension, Uric Acid levels were significantly higher in these patients and between Uric Acid levels and increased pulmonary arterial resistance which was consistent with the results of our study. In a study by Oya et al. in Japan in 2000 that was done on 49 patients with Eisenhower, increased Uric Acid levels correlated with increased pulmonary arterial pressure increased mortality and decreased EF. Reducing GFR may increase pulmonary arterial pressure, but there was no direct correlation between them in our study. Another study by X.R.Bao and Q.M.yang[14] conducted in China in 2014 on 101 patients with chronic renal failure, the PHTN incidence was significantly higher than GFR <60. However, in our study, all patients had a GFR of <60 (stage 3a, 3b, 4), and in these stages, there was no relationship between GFR reduction and pulmonary arterial hypertension. In a study by Zhilian La et al.[20] in 2010-2008, the group with PHTN had higher age, lower GFR, lower EF, and lower Hb. In the Yang study,[14], the group had higher PHTN, MAP, higher age, and lower EF, but no correlation was found between sex and BMI and no PHTN. In Oya, there was a significant relationship between the incidence of PHTN and EF. Regarding our findings and the findings from similar studies, Uric Acid levels seem to be considered a risk factor for PHTN and a risk factor for mortality. Similarly, according to previous studies, in the presence of PHTN, even if patients have kidney transplants, they increase the motor mobility of patients.[11,16] Considering the costs involved in kidney transplantation and the treatment system, the risk factors for the onset of PHTN and their timely treatment can have a positive effect on reducing mortality. On the other hand, an increase in pulmonary arterial pressure in patients with chronic renal failure can be due to left ventricular dysfunction. Risk factors for chronic kidney diseases such as volume overload, arteriovenous fistula in the form of dialysis,[6] contact with dialysis membranes,[7] Sleep and respiratory disorders,[8] endothelial dysfunction,[9] and calcification and rigidity of the arteries and severe anemia[10] are created or exacerbated.

5. Conclusion

In our study, there was no significant relationship between the incidence of PHTN and EF. There was no significant relationship between age, sex, SBP, DBP, BMI, and PHTN. An increase in pulmonary arterial pressure in patients with chronic renal failure can be due to left ventricular dysfunction. Therefore, in addition to controlling the level of Uric Acid, treatment of HTN, DM, anemia, calcium, and phosphorus disorders, volume overload can reduce the risk of developing PHTN.

Conflict of Interest

The authors declared that there is no conflict of interest.

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