Uremic Pruritus Characteristics in Hemodialysis Patients with Chronic Kidney Disease in Relation to Blood Urea Levels and Dialysis Adequacy at Jakarta Pelabuhan Hospital, Indonesia

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Abstract: Background and objective: Uremic pruritus is one of the distressing symptoms encountered in patients with chronic kidney disease. It compromises overall quality of life. Factors associated with the severity of pruritus remains unclear. This study aims to describe and analyze the relationship of blood urea level and dialysis adequacy to uremic pruritus. Methods: We conducted a cross-sectional study for 3 months at Jakarta Pelabuhan Hospital, Indonesia. The intensity of uremic pruritus was measured using both visual analog scale (VAS) and numerical rating scale (NRS). Results: Of the 75 patients completed the study, 30 (40%) had pruritus. There was no significant correlation between uremic pruritus and blood urea level as well as dialysis adequacy ($p>0.05$). Conclusion: Our study suggests that blood urea level and dialysis adequacy do not play a role in pruritus in hemodialysis patients with chronic kidney disease.

1 INTRODUCTION

Uremic pruritus is one of the most frequent complications found in hemodialysis patients with chronic kidney disease. The itch of uremic pruritus, whether localized or disseminated, is debilitating for the majority of patients. This intractable symptom could lead to affect patients' quality of life (Ko et al., 2013). Fifty to ninety percent of hemodialysis patients with chronic kidney disease are afflicted with pruritus (Akça & Taşci, 2014; Al Shafei & Nour, 2016). There are multifactorial factors that could cause uremic pruritus, in particular, blood urea levels. Previous studies suggested that uremic pruritus is significantly correlated with elevated levels of blood urea (Al Shafei & Nour, 2016). On the contrary, an effective dialysis has been shown to reduce the severity of uremic pruritus (Ko et al., 2013).

To the best of our knowledge, there were no studies in Indonesia reporting the prevalence of uremic pruritus in hemodialysis patients with chronic kidney disease as well as its correlation to blood urea levels and dialysis adequacy. We hence sought to describe the prevalence and clinical characteristics of uremic pruritus in hemodialysis patients with chronic kidney disease in Jakarta Pelabuhan Hospital, Indonesia. Our research additionally investigates the associations of blood urea levels and dialysis adequacy with the severity of uremic pruritus measured by means of visual analog scale (VAS) and numerical rating scale (NRS).

2 METHODS

This was an analytical descriptive study of patients with chronic kidney disease undergoing hemodialysis treatment at Jakarta Pelabuhan Hospital Hemodialysis Unit. We conducted a cross-sectional research commencing from September 27th, 2017 until December 27th, 2017. The inclusion criteria of our study comprised of age above 18 years, no history of mental health problems as well as consent to participate. The study population was obtained using a consecutive sampling technique and was excluded if the patient did not give written consent.

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During this 3-month period of study, a total of 76 patients were receiving hemodialysis treatment at the hospital hemodialysis unit. However, one patient was excluded because of the patient's refusal. Thus, 75 patients were included in our final analysis. Subjects received 3.0 – 5.0 hours of hemodialysis, one to three times a week using bicarbonate dialysate and heparin anticoagulant. In case of allergy, we switched heparin to enoxaparin sodium or parnaparin. The diagnosis of uremic pruritus was made if patients met one of the following criteria: appearance of pruritus shortly before the dialysis treatment or at any time of dialysis without evidence of any other active causes of pruritus; a minimum of 3 episodes of troubling pruritus that appears a couple times in a day and lasts at least a few minutes during a period of time less than 2 weeks; pruritus appears less frequently than aforementioned criteria but in a regular pattern in a period of 6 months (Keithi-Reddy et al., 2007).

We designed a comprehensive questionnaire to evaluate the clinical characteristics of uremic pruritus and to assess the dialysis adequacy. In regard to the measurement of the pruritus severity, we used two different validated tools, VAS and NRS (Phan et al., 2012; Reich et al., 2016; Reich et al., 2012). Patients were asked to point to the 10-cm horizontal line of VAS that corresponded to the intensity of pruritus where the starting point (0 cm) indicated no pruritus and the last point (10 cm) demonstrated the worst imaginable pruritus. We further asked patients to tell verbally a NRS score that best reflected their symptom severity where 0 was no pruritus and 10 represented intolerable pruritus. The laboratory parameter, blood urea level, was measured before the beginning of hemodialysis treatment. We applied the Kt/V ratio (amount of dialysis delivered: K = clearance of urea, t = time on dialysis, V = estimated total body water) to measure the adequacy of dialysis; Kt/V > 1.5 was considered as an effective dialysis (1). Statistical analysis was performed using IBM SPSS Statistics software version 23.0 where statistical significance was defined by a probability level of $p < 0.05$ (95% confidence interval). Descriptive data were expressed as a mean ± standard deviation and percentage. Mann-Whitney-U and t-test were performed to compare means between pruritic and non-pruritic patients.

3 RESULT

A total of 75 patients participated in this study. Patients' demographic and clinical characteristics, as well as blood urea levels are summarized in Table 1. The average age of the patients was 56 ± 12,6 years, ranging from 33-87 years with 65% being males and 35% being females. In pruritic patients, there were 18 male patients (60%) and 12 female patients (40%). Table 2 demonstrated the prevalence and uremic pruritus characteristics. The most frequent pruritus distributions were the localized areas (77%) consisted of the back (32%), the head (17%), followed by other areas including the chest, palm, arm, crotch, waist, thigh, sole, back of hand, shoulder, stomach, and elbow. There was no statistically significant difference in the blood urea levels between pruritic patients (n = 30, Md = 115.00) and non-pruritic patients (n = 45, Md = 111.00) according to the Mann-Whitney-U test (p = 0.669) . Applying the non-dependent t-test, we found that the means of dialysis adequacy in 30 patients with uremic pruritus and 45 patients without pruritus were not statistically significantly different (p = 0.192).

Table 1. Demographic, clinical characteristics, and blood urea levels of the participants

Variables		Pruritic patients (n=30)	Non-pruritic patients (n=45)
Gender	Male	18 (60%)	31 (69%)
	Female	12 (40%)	14 (31%)
Age (years)		54 ± 13.0	57 ± 12.3
Etiology of chronic kidney disease			
Hypertension (HTN)		11 (37%)	19 (42%)
Diabetes mellitus (DM)		5 (17%)	11 (24%)
Kidney stone		-	3 (7%)
Polycystic kidney disease		1(3%)	1 (2%)
Idiopathic		3 (10%)	2 (5%)
Others		1 (3%)	-

Combined	DM with HTN	8 (27%)	7 (16%)
	HTN with others	1 (3%)	1 (2%)
	HTN with kidney stone	-	1 (2%)
	Polycystic kidney disease with others	-	-
Duration of hemodialysis	≤ 3 months	7 (23%)	22 (49%)
	>3 months	23 (77%)	23 (51%)
Dialysis adequacy (Kt/V)		2.3 ± 0.9	2.0 ± 1.1
Dialyzer membrane	Polysulfone	21 (70%)	22 (49%)
	Polyarylethersulfone	9 (30%)	23 (51%)
Hemodialysis acces	Continuous	21 (70%)	21 (47%)
	Temporary	9 (30%)	24 (53%)
Blood urea levels		112.8 ± 34.5	125.5 ± 58.6

Abbreviation: n: Number of patients, K: clerarance of urea; t: time on dialysis; V; estimated total water

Table 2. Uremic pruritus characteristic in patients with pruritus

Variables		Statistics
Uremic pruritus diagnosis criteria	Apperance of pruritus shortly before the dialysis treatment or at any time of dialysis without evidence of any other active causes of pruritus	11 (37%)
	A minimum of 3 episodes of troubling pruritus that appears a couple times in a day and lasts at least a few minutes during a period of time less than 2 weeks	15 (50%)
	Pruritus appears less frequently than aforementioned criteria but in a regular pattern in a period of 6 months	4 (13%)
Distribution	Generalized	7 (23%)
	Localized	23 (77%)
Numerical Rating Scale (NRS)		4,5 ± 2.3
Visual Analog Scale (VAS)		4 ± 2.1

Abbreviation: n: Number of patients

4 DISCUSSION

Uremic pruritus remains a frequent and intractable symptom encountered in hemodialysis patients with chronic kidney disease (Ko et al., 2013; Kilic & Tasci, 2014, Shirazian et al., 2017). There is inconclusive evidence in terms of the pathophysiology of this entity. In our study, we found that there were 40% patients with chronic kidney disease experiencing uremic pruritus. From this 30 pruritic patients, 18 were males and 12 were females. From this 30 pruritic patients, 18 were males and 12 were females. The majority of patients who reported pruritus were those who had already undergone hemodialysis treatment for more than 3 months (77%).

Fifteen percent of pruritic patients met the second diagnosis criteria of uremic pruritus which was a minimum of 3 episodes of troubling pruritus that appears a couple times in a day and lasts at least a few minutes during a period of time less than 2 weeks. Unlike our study, most of previous studies did not analyze the prevalence of uremic pruritus specifically based on the diagnosis criteria of uremic pruritus according to its time of onset and episode frequency.

Narita et al reported that blood urea level was statistically correlated with pruritus severity. According to Ko et al's study, dialysis adequacy 1.5 had a significant effect in decreasing the severity of pruritus. On the other hand, we found a difference in blood urea levels between pruritic and non-pruritic groups but it was not statistically significant $p > 0.05$ (0.669). Our study also showed that there was no statistical difference regarding dialysis adequacy (Kt/V) between the two groups ($p > 0.05$). These findings could be affected by the small number of participants in our study.

There were 23 pruritic patients (50%) from a total of 46 patients who had received hemodialysis treatment for > 3 months. For 29 other patients who had undergone hemodialysis for ≤ 3 months, 7 of them (24%) had pruritus. Until now, the relationship of dialysis vintage with uremic pruritus was controversial. Some studies suggested that 3-month hemodialysis therapy would result in decreased intensity of pruritus while others reported that a minimum of 12-month hemodialysis would show beneficial effect. The most common used pruritus assessment tools are VAS and NRS attributed to its high discriminative sensitivity. According to the study from Reich et al, evaluation with NRS would result in higher pruritus intensity compared with VAS. There was only a slight difference of 0.1 – 0.6 points between VAS and NRS assessment but this was not statistically significant (Reich et al., 2012; Reich et al., 2016). In our study, the pruritus intensity in the 30 patients with pruritus was 4 ± 2.1 and 4.5 ± 2.3 for VAS and NRS scores, respectively. With regard to the distribution of the pruritus, we found that 77% of the patients had localized pruritic areas on the back, head, chest and extremities. Our findings were consistent with data regarding the high variety of the uremic pruritus distribution with the most commonly involved areas were back, stomach, hand and head.

5 CONCLUSION

Taken together, our study demonstrates that there is no statistically significant correlation between uremic pruritus and blood urea level or dialysis adequacy. However, there are some limitations of this study. First, a small number of participants were involved. Second, the data on VAS and NRS did not include the baseline scores before the hemodialysis treatment started. Therefore, we could not further analyze the relationship of dialysis adequacy and reduction of pruritus. Third, our study did not exclude participants with confounding factors, for instance diabetic and hepatitis patients. Further research with bigger sample size and prospective design is necessary to understand contributing factors in uremic pruritus development.

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