

## Risk Factors Of Uremic Pruritus In Hemodialysis Patients :Narrative Literature Review

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### Abstract

Uremic pruritus is a dermatological manifestation that common and disturbing problem in patients undergoing hemodialysis with an incidence of 20% - 90%. The pathogenesis of uremic pruritus is complex and incompletely understood. This review study aimed to identify factors of uremic pruritus in hemodialysis patients. A literature review searched three database (Proquest, NCBI, and Google Scholar) for previous studies using cross sectional, case control, and descriptive kuantitative desaign published between 2015-2020. The PRISMA checklist guided by year, title, abstract, and full text. The JBI Critical Appraisal Tools are used to assessing the quality of articles. A total of ofthirteen articles which met inclusion criteria in this study. Each article identified a different risk factor for uremic pruritus with at least one risk factor identified by the two articles. The majority of study designs were cross-sectional with eleven articles. The average number of participants were more than fifty. A total of five risk factors that contributing of uremic pruritus: 1) clinical features (increased urea, creatinin, hemoglobin, protein C reaktif, Interleukin (IL)-2 dan Interleukin (IL)-6), 2) dialysis adequacy, 3) duration of hemodialysis, 4) gender, and 5) age. Increased of urea level were indicated as the most dominant risk factor because it acts as an intermediary for others.

**Keywords:** clinical features, hemodialysis, risk factors, uremic pruritus

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### I. Introduction

Chronic Kidney Disease (CKD) is a systemic disease that has many clinical signs. Glomerular Filtration Rate (GFR) is <15 mL / minute / 1.73m<sup>2</sup>, it is included in category of kidney failure, which it is a condition where the kidneys unable to carry out their main function as an excretory system (Rachmadi, 2017). In this condition, therapy needs to be done to sustain the patient's life, namely by maintaining the resistance of the process of removing metabolic waste (Widianti, 2017).

Hemodialysis (HD) is the most preferred therapy for CKD patients other than peritoneal dialysis and kidney transplants (Haryanti, I. A. P., 2015). Among other therapies, hemodialysis is more accessible and is believed to be able to sustain a patient's life longer (Bayhakki & Hasneli, 2017). However, this therapy does not guarantee that patients will avoid a number of other potential health problems. Pruritus is a common problem complained of by hemodialysis patients with a high incidence rate of up to 90%.

Pruritus is defined as an unpleasant sensation on the skin area which then triggers the urge to scratch (Rachmadi, 2017). Meanwhile, pruritus that occurs in chronic kidney failure is defined as an unpleasant feeling on the skin which is probably caused by the accumulation of toxic uremia due to kidney failure to excrete protein metabolic waste (Wu, 2015).

The incidence of uremic pruritus is high and even triggers an increase in mortality. Grochulska (2019) cohort study of 724 hemodialysis patients with itching recorded from 2013 - 2017, as many as 48.1% had died accompanied by skin lesions due to itching. This mortality rate is related to the intensity of itching that causes depression, stress, and sleep disturbances (Grochulska, 2019). A recent study by (Kumar, 2020) on 59 HD patients, as many as 37 (63%) had pruritus. Likewise research by Kadam (2018) on 77 samples, showed that more than half of the sample (57.2%) complained of pruritus. Research in Indonesia also shows that pruritus is experienced by the majority of HD patients. Wahyuni (2019) stated that out of 83 HD patients, 73 (89%) had pruritus.

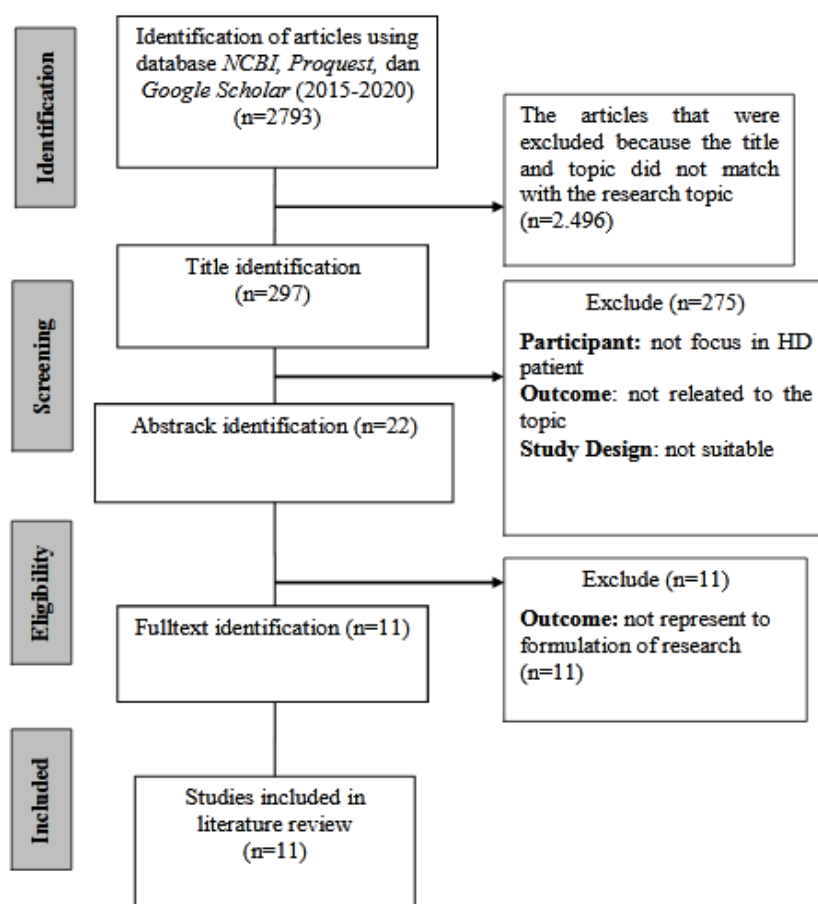
With a relatively high incidence rate, pruritus should be a concern and maximum management should be done. However, in reality the treatment of pruritus is not yet effective because the factors of pruritus are not clear. Hu (2019), in the conclusion of their research said that it is very difficult to say that pruritus is caused by a single factor. Based on these results, the researcher is interested in conducting a literature review to determine and summarize the risk factors for the appearance of uremic pruritus in patients undergoing hemodialysis.

## II. Method

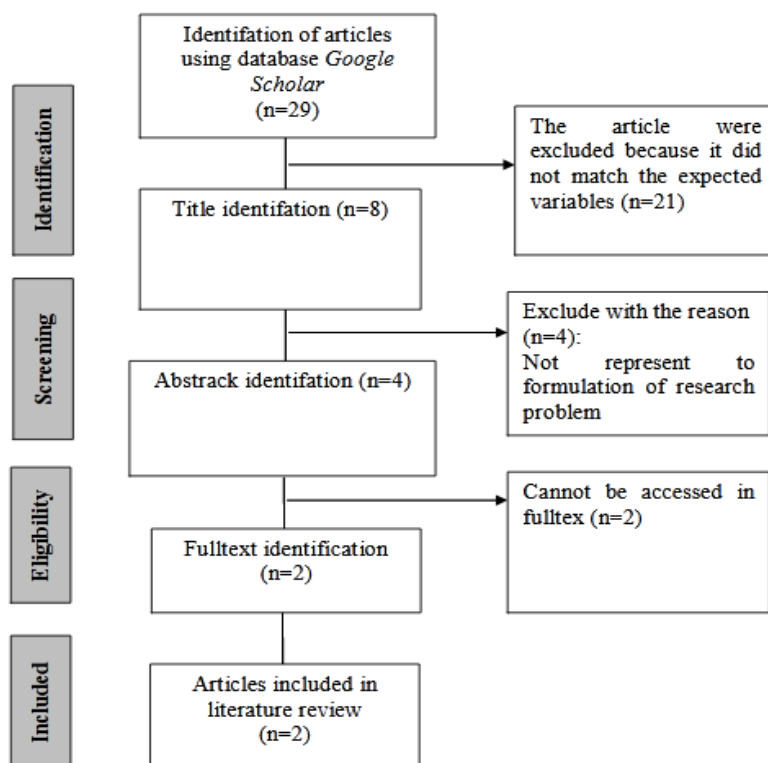
This research used narrative literature review method. The process of searching for articles were carried out through databases including the National Center for Biotechnology Information (NCBI), Proquest, and Google Scholar. Articles are searched using English and Indonesian key words adjusted to the Medical Subject Heading (MeSH) and boolean operators (AND, OR NOT or AND NOT).

The English keywords defined are ("Factor" OR "Risk Factor" OR "Causality") AND ("Biochemical Parameters" OR "Clinical Features" OR "Interleukin") AND ("Uremic Pruritus" OR "Pruritus" OR "Severity of Pruritus "OR" Itch ") AND (" Hemodialysis "). These keywords were entered in the National Center for Biotechnology Information (NCBI), Proquest, and Google Scholar databases. Meanwhile, the Indonesian keywords are ("Hemodialysis" OR "Long Underwent Hemodialysis") AND ("Uremic Pruritus") AND ("Chronic Kidney Failure" which is entered into the Google Scholar database.

Flow diagram are used as a guide in the process of searching for articles. The flow diagram for each keyword is independent, for English keywords (Figure 1) and Indonesian (Figure 2). The articles found were then evaluated for quality based on The JBI Critical Appraisal Tools. Inclusion criteria were determined based on PICOS guidelines, including: 1) CRF patients who undergo HD, 2) Hemodialysis, 3) HD patients with pruritus or nonpruritus, 4) Cross sectional study, Case control study, descriptive quantitative, 5) publication year 2015-2020, 6) English and Indonesian Language.



Gambar 2.1 Flow Diagram of Articles Selection with English Language Key Word



Gambar 2.2 Flow Diagram of Articles Selection with Indonesia Language Key Word

### III. Result

From the two process of searching articles using keywords in English and Indonesian language, researchers got a total of 13 articles. A total of 13 articles were then taken and set for analysis as the basis for a literature review study. The followings are summary if articles that had been analyzed (Tabel 1).

Table 1. Summary Of Articles

Author	Title and Identity of Article	Method (Design, Sample, Variable, and Analysis)	Result of Analysis
Hu, T., at. al (2019)	<b>Title:</b> Clinical features and risk factors of Experimental And Therapeutic Medicine pruritusin patients with chronic renal failure. <b>Identity:</b> 18: 964-971, 2019 Doi: 10.3892/Etm.2019.7588	<b>D:</b> Cross-sectional study <b>S:</b> 382 patients: 138 HD, 41 Dialisis peritoneal, 203 CKD <b>V:</b> socio demographics, clinical parameters (serum urea nitrogen, creatinine, serum phosphorus, calcium phosphorus, and parathyroid hormone (PTH) <b>A:</b> Chi-square test was used for comparisons of numerical variables.	Of the two groups, hemodialysis and peritoneal dialysis, pruritus was most prevalent in the HD group with a total of 96 versus 25 pruritus patients. Risk factors: The intensity of pruritus was correlated with increased levels of serum urea nitrogen, creatinine, serum phosphorus, and calcium (p <0.001).  Significance value p <0.05 and high significance p <0.01.
Shafei, N. K dan A. Nour. (2016)	<b>Title:</b> Observations on the Association of Serum histamine, Interleukins and Other Serum Biochemical Values with Severity of Pruritus in Chronic Hemodialysis Patients <b>Identity:</b> Journal of nanomedicine & Nanotechnology	<b>D:</b> Cross-sectional study <b>S:</b> 50 hemodialysis patients <b>V:</b> uremic pruritus and clinical parameters <b>A:</b> comparison with the ANOVA test	BUN (urea) and creatinine values are increased or higher in patients with severe pruritus. This is shown by the comparison of pruritus values for the control group (without HD), HD with no pruritus, and HD with mild to moderate pruritus. High values of potassium levels were also found in the moderate to severe pruritus group. Histamine values were found to be significantly increased in HD and pruritus patients. The increase occurred in severe pruritus, while the mild pruritus group had the lowest histamine levels. Cortisol is found to be high in patients with moderate pruritus, but decreased or lower in patients with severe pruritus. Interleukin-2 values increased but not significantly between HD patients and pruritus compared to

			controls. whereas Interleukin-6 was increased in patients with moderate pruritus. P value <0.05.
Odonmeta, B. A., E. Unuigbo, dan C. I. Otene (2016)	<b>Title:</b> Pruritus in Patients on Maintenance Hemodialysis in Benin City, Edo State, Nigeria <b>Identity:</b> Journal of Integrative Nephrology and Andrology October-December 2016 Vol 3 Issue 4 DOI: 10.4103/2394-2916.193498	<b>D:</b> cross sectional study <b>S:</b> 50 hemodialysis patients <b>V:</b> uremic pruritus and clinical parameters <b>A:</b> Pearson for assess the association between pruritus and clinical parameters.	Of the 50 hemodialysis patients, 24 (48%) had pruritus. Clinical parameters that have been shown to be associated with pruritus are serum urea, increasing age, anemia, and HD duration.
Oliveira, M. G., at al. (2017)	<b>Title:</b> Factors Associated with Uremic Pruritus <b>Identity:</b> International Archives of Medicine Vol. 10 No. 178 doi: 10.3823/2448	<b>D:</b> cross sectional study <b>S:</b> 164 hemodialysis patients over 18 years old <b>V:</b> uremic pruritus, demographics, and clinical value <b>A:</b> Multivariate linear regression test	From a total of 164 samples, 64 experienced pruritus. Based on the multivariate analysis, increased creatinine and decreased hemoglobin levels were risk factors for uremic pruritus, with p = 0.048 and p = 0.043, respectively. Significance value p <0.05
Ghassan, B at al. (2015)	<b>Title:</b> Relationship of Pruritus with Biochemical and Haematological Parameters in Haemodialysis Patients (A Single Center Study) <b>Identity:</b> J Fac Med Baghdad Vol. 57 No. 4	<b>D:</b> cross sectional study <b>S:</b> 103 hemodialysis patients <b>V:</b> uremic pruritus and clinical parameters <b>A:</b> -	From 103 hemodialysis patients, 79 patients experienced pruritus with different intensities. Clinical values did not show any significant difference except for hemoglobin values (r = 0.283, p = 0.011). There was a significant correlation between increase of age and uremic pruritus (r = 0.288, p = 0.010).  Significance value p <0.05.
Sarhan, I. I., at. al. (2020)	<b>Title:</b> Association Of High Sensitive C Reactive Protein And Dialysis Adequacy With Uremic Pruritus In Hemodialysis Patients <b>Identity:</b> Alexandria Journal Of Medicine 2020, Vol. 56, No. 1, 111–117 Doi:1080/20905068.2020.1786620	<b>D:</b> Case control study <b>S:</b> 100 hemodialysis patients: 50 Patients HD with pruritus dan 50 nonpruritus. <b>V:</b> demographic data, adequacy of dialysis, uremic pruritus <b>A:</b> Chi-squares were used for group comparisons of qualitative data. Independent t-test for comparison of independent groups with quantitative data and parametric distribution. Mann-Whitney was used for comparison of non-parametric distribution data.	The results of researching showed that there was a negative but significant correlation between adequacy of hemodiaysis and uremic pruritus as measured by the Urea Reduction Ratio (URR) value (p value = 0.017). There was a positive and significant correlation between CRP and pruritus (p = 0.001).  Significance value p <0.05.
Malekmakan, L., at. al. (2015)	<b>Title:</b> Association of High-Sensitive C-Reactive Protein and Dialysis Adequacy with Uremic Pruritus <b>Identity:</b> Saudi Journal of Kidney Diseases and Transplantation, Vol. 26 No. 5 Hal. 890-895	<b>D:</b> Case control study <b>S:</b> 241 patients aged ≥18 years and having undergoing HD ≥3 months <b>V:</b> uremic pruritus, demographic data, and clinical value (Kt/V or hemodialysis adequacy) <b>A:</b> Independent t test for quantitative data test and Chi-square for comparison.	Of the study sample, 40.2% (97) had pruritus. There were no significant differences in laboratory values between pruritic and non-pruritic patients, except for Kt / V and CRP values. Kt / V values were significantly higher in pruritic patients (p <0.001). CRP values were found to be significantly higher in patients with pruritus compared with non-pruritic patients (P = 0.004). Significance value p <0.05.
Rusyati, Y. Kandarai, dan N. T. Piliawati (2020)	<b>Title:</b> High serum interleukin-2 levels are associated with pruritud in chronic kidney disease undergoing regular hemodialysis <b>Identity:</b> Bali Medical Journal Vol. 9 No. 3 doi: 10.15562/bmj.v9i3.2018	<b>D:</b> Cross-sectional study <b>S:</b> 72 hemodialysis patients: 36 with pruritus and 36 without pruritus <b>V:</b> characteristics (age, sex, HD duration) and serum interleukin-2 <b>A:</b> Normality test with Kolmogorov Smirnov, Independent t-test for interleukin-2 differences between groups	Comparative analysis showed that the CKD group with pruritus had higher serum IL-2 than the CKD group without pruritus (17.1 ng / mL versus 13.0 ng / mL; p <0.001).  Significance value p <0.05
Abdelsalam, M., at al (2019)	<b>Title:</b> Insulin Resistance and Hepatitis C Virus-Associated Subclinical Inflammation Are Hidden Causes of Pruritus in Egyptian Hemodialysis Patients: A Multicenter Prospective Observational Study <b>Identity:</b> Nephron DOI: 10.1159/000501409	<b>D:</b> Cross-sectional study <b>S:</b> 193 hemodialysis patients <b>V:</b> risk factors and uremic pruritus <b>A:</b> Shapir-Wilk for normality. Comparison of the two groups t-test (parametric data) and Mann-Whitney (non-parametric). ANOVA for comparisons of more than two groups. Spearmen to assess the relationship between	Pasien pruritus jauh lebih dominan dari nonpruritus (164 vs 47). Terdapat hubungan signifikan secara statistik antara usia (p=0,002), durasi HD (p=0,036), serum feratinin (p=0,003), fosforus (p=0,0001), CRP (p=0,0001), insulin (p=0,0001), dan Kt?V (p=0,0001).Berdasarkan uji linear multivariat menunjukkan prediktor pruritus yaitu usia, durasi HD, fosforus, Kt/V, CRP (p=0,004, p=0,0001, p=0,0001, dan 0,013). Nilai statistik signifikansi p<0,05 dan

	variables.	signifikansi tinggi p<0,0001.
Kaur, S., at al (2019)	<b>Title:</b> Prevalence of Uremic Pruritus, Its Risk Factors and Impact on Health-Related Quality-Of-Life in Patients on Maintenance Hemodialysis <b>Identity:</b> Academia Journal of Medicine Vol. 2 No. 2	<b>D:</b> Cross-sectional study <b>S:</b> 164 hemodialysis patients <b>V:</b> risk factors and uremic pruritus <b>A:</b> Annova test for comparison of quantitative data and Chi-square test for comparison of categorical data.
Vrucinic et al., (2015)	<b>Title:</b> Pruritus In Hemodialysis Patients: Results From Fresenius Dyalisis Center, Banja Luka, Bosnia And Herzegovina <b>Identity:</b> Our Dermatol Online. 2015;6(3):252-256	<b>D:</b> Cross-sectional study <b>S:</b> 62 hemodialysis patients <b>V:</b> uremic pruritus, age, sex, HD duration, and laboratory characteristics <b>A:</b> Mann-Whitney and t-test to compare between patients with or without pruritus. Wilcoxon and Chi-square test to assess of correlation of variables
Wahyuni, A.,U. Z. Lawati, dan E. Gusti (2019)	<b>Title:</b> Korelasi Lama Menjalani Hemodialisa Dengan Pruritus Pada Pasien Hemodialisa <b>Identity:</b> Jurnal Endurance : Kajian Ilmiah Problema Kesehatan Vol 5 No 1	<b>D:</b> cross sectional study <b>S:</b> 83 hemodialysis patients <b>V:</b> Duration of hemodialysis and uremic pruritus <b>A:</b> Chi square for assess the correlation of variable
Sembiring, F., S. S. Nasution, dan Y. Ariani (2020)	<b>Title:</b> GambaranPruritusUremikPasiennGagalGinjalKronikDiUnitHemodialisaRumahSakitUmumPusatHajiAdam Malik Medan <b>Identity:</b> Jurnal Perawat Indonesia Vo. 4 No. 1	<b>D:</b> descriptive quantitative <b>S:</b> 49 hemodialysis patients <b>V:</b> uremic pruritus <b>A:</b> -

#### IV. Discussion

##### 1. Clinical Features

###### 1.1 Urea

Uremia is the most common cause of pruritus because it has a fairly clear pathogenesis. Accumulated urea levels in the blood can endanger the patient's survival and interfere with the hemodialysis therapy process. Increased levels of urea in the blood can be a factor in the emergence of uremic pruritus in hemodialysis patients. Urea, which should be excreted in the urine in the metabolic process, is deposited so that it becomes toxic to the detriment of patients. Increased urea levels were found to be high in pruritic patients and it was found that urea levels had a statistical relationship with the incidence of pruritus intensity ((Odometa, B. A., E. Unuigbe, 2020);(Shafei, N. K., 2016);(Hu, 2019).

Research in Nigeria by Odonmeta (2016) on 50 hemodialysis patients, as many as 48% of them experienced pruritus with urea levels far above normal values, namely 252.1 mg / dL. These results indicated that the increase in serum urea levels was associated with the frequency of pruritus (p = 0.001). The uncontrolled increase in urea levels was caused by the patient not undergoing hemodialysis therapy regularly due to the cost factor that was borne by the patient himself. The irregularity of patients undergoing HD therapy causes the process of eliminating metabolic waste to stop as a result of which urea becomes one of the accumulated metabolic waste.

###### 1.2 Creatinine

Creatinine in the blood is constant, namely 0.6 - 1.3 mg / dL, but this value will increase when there is a decrease in kidney function. Creatinine is excreted by the renal glomerulus, so an increase in serum creatinine value has a relationship with a decrease in Glomerular Filtration Rate (GFR) as the level of kidney damage. According to Olivevera (2017), HD patients with pruritus have a higher creatinine value than the HD group without pruritus. This indicates that kidney function will affect creatinine excretion so that the accumulation occurs in the blood and becomes a risk factor for pruritus.

The results of research by Oliveira (2017) reported that creatinine in pruritic patients was in the range of 7.4 to 11.6 mg / dL with an average of 9.9 mg / dL, while in the group without pruritus, creatinine levels were also above the normal value, namely the range of 6 , 6 -10.6 mg / dL. Although the creatinine level in the group

without pruritus was also high, the difference with the pruritus group indicates that creatinine is a risk factor for pruritus.

Hu et al. (2019) reported that in pruritic patients, the creatinine value was 793  $\mu\text{mol} / \text{l}$  versus 570  $\mu\text{mol} / \text{l}$  in non-pruritic patients (normal creatinine in  $\mu\text{mol} / \text{l}$  was 80-115  $\mu\text{mol} / \text{l}$ ). The results of this study indicate that an increase in creatinine value will cause the occurrence of pruritus.

### **1.3 Hemoglobin**

The process of abnormal hemoglobin levels associated with uremic pruritus is not fully understood. One of the pathophysiologies that can be proposed for the theory of the emergence of pruritus is that hemoglobin is related to the incidence of anemia in dialysis patients (Pisoni,2006). When the production of red blood cells is insufficient, the process of spreading hemoglobin will be hampered so that the cells in the body are disrupted including glomerular function because erythropoietin is produced in the peritubular capillary endothelial cells of the kidney cells. This situation will affect the emergence of toxic buildup in the body and complications that can arise are uremic pruritus (Olievera, 2017).

### **1.4 Interleukin (IL)-2 dan Interleukin (IL)-6**

Serum Interleukin (IL) -2 and Interleukin (IL) -6 are indicated as risk factors for uremic pruritus because they are associated with inflammation. (Kimmel, 2006) study of 13 pruritic patients showed that IL-2, IL-6, and CRP were found to be higher in hemodialysis patients with pruritus than in hemodialysis patients without pruritus. The cytokines IL-2 and IL-6 are important immunoregulators and neuroregulators in the central nervous system. The cytokines IL-2 and IL-6 can affect the physiological function of nerve cells and modulate several neurotransmitter systems in the central nervous system, thereby resulting in changes to higher CNS function. This condition can then cause neurological effects and neuropsychiatric symptoms in the form of itching or pruritus (Gaspari, 1987 in (Fallahzadeh, 2011). According to Shafei, N. K. (2016)and Rusyati, 2020),interleukin-2 and 6 are associated with uremic pruritus.

Another study by Rusyati (2020) related to IL-2 with pruritus showed that in pruritus patients there was an increase in IL-2 values to 17.1 pg / ml while the value for patients without pruritus was 13 pg / ml (still in the normal range of 5-15 pg / ml). The results of this study concluded that there was a statistical relationship between an increase in serum interleukin-2 values and pruritus in hemodialysis patients.

### **1.5 Protein C Reaktif (CRP)**

Serum CRP is an important marker in identifying inflammation in several chronic diseases. CRP itself has a role in the emergence of uremic pruritus with inflammation as the suspected pathway. According to research by Chiu (2008),severe pruritus had significantly higher serum CRP levels (mean = 4.22 mg / L, ideal CRP value = 1.00-3.00 mg / L; p = 0.017) . Logistic regression analysis showed that high CRP levels were meaningful as independent predictors of uremic pruritus with adjustments for gender, age, and dialysis duration (Chiu, 2008).

Likewise research by Sarhan et al. (2020) who also stated that the CRP value is associated with uremic pruritus. Highly sensitive reactive protein C was statistically positively correlated with the intensity of uremic pruritus as measured by a visual analog scale (p value = 0.001). Research Abdelsalam, M., at. al (2019) also reported that CRP was a predictor of pruritus (p <0.0001).

## **2. Hemodialysis Adequacy**

The increase of urea can be caused by other factors, such as adequate hemodialysis. Ineffective adequate hemodialysis will affect the amount of urea in the body. Hemodialysis patients with lower URR values have a strong potential to experience uremic pruritus (Sarhan et al., 2020). Research by Sarhan et al., (2020) on 241 HD patients, as many as 97 (40.2%) patients had pruritus. Sarhan reported that the ratio of URR values between pruritic and non-pruritic patients was 63% versus 60%.

Likewise, the results of research from Malekmakan et al., (2015) stated that there was a relationship between adequate hemodialysis and uremic pruritus. Among other variables in the study, such as demographic data and body mass index, there was no correlation with pruritus, that is, there was no difference between the pruritus and non-pruritic groups. The differences between groups appeared in the urea clearance values. Lower ure clearance values (> 1.2) were significantly associated with the appearance of uremic pruritus among hemodialysis patients (Malekmakan et al., 2015). The same result was also reported by Abdelsalam, M., at. al (2019), namely the value of urea clearance (Kt / V) in pruritic patients was higher than nonpruritic patients (1.3 vs 1.5) with a significance value (p = 0.0001). This value indicates that improved dialysis adequacy reduces the risk of dialysis patients experiencing pruritus.

### **3. Duration of Hemodialysis**

Several studies have shown that the length of time undergoing hemodialysis has a role in the appearance of uremic pruritus. Research by Wahyuni, A., et al (2018) on 83 hemodialysis patients showed that 78 of them had pruritus with an average length of undergoing hemodialysis being 21 months. The results of the bivariate analysis showed that there was a relationship between the two, where the correlation coefficient was positive, which meant that there was a relationship between the length of hemodialysis and the incidence of pruritus ( $p = 0.023$ ).

Other studies that support the assumption that the length of time undergoing hemodialysis is a risk factor for the appearance of pruritus reported by Sembiring, F., et al. (2020) and Odonmeta, B. A., E. Unuigbe, C. I. Otene (2016), and Abdelsalam, M., at. al (2019). Sembiring, F., et al (2020) analyzed the picture of pruritus in 49 hemodialysis patients and found that all samples had mild pruritus and the majority had undergone hemodialysis for more than one year. Of the 49 respondents observed, 39 respondents had complained of itching for more than 6 months.

Odonmeta, B. A., E. Unuigbe, and C. I. Otene (2016), stated that patients with increased duration have a risk of developing pruritus because of the risk of skin disorders. These results indicate that the length of time on hemodialysis has a greater potential for patients to experience pruritus. Abdelsalam, M., at. al (2019) also stated the same thing that patients who had longer undergone HD pruritus had pruritus than patients who were shorter (36.5 months vs 27 months).

### **4. Gender**

Sex differences have also been of concern to some investigators regarding the development of CKD and its association with uremic pruritus. Research by Vrucinic et al., (2015) regarding the correlation between pruritus and its risk factors was examined from 62 HD patients and it was found that 27 (45.2%) had pruritus. From the sex comparison, pruritus appeared more in men, namely 21 of 34 patients (54.8%) compared to 6 of 22 patients (45.2%) in women. The correlation between pruritus and other variables such as age, HD duration and laboratory values did not show any significant association. Male gender had a significant correlation with the appearance of pruritus ( $p = 0.005$ ). Vrucinic et al., (2015) concluded that gender can be a risk factor for the emergence of pruritus but how the mechanism is not explained with certainty.

Research in Indonesia by Sembiring, F., et al (2020), also showed that male hemodialysis patients had more pruritus than women. Of the 49 respondents who were observed, as many as 30 (61.2%) experienced pruritus. This study concluded that gender has a role in the emergence of pruritus with male gender as a vulnerable group.

### **5. Age**

Older people are considered susceptible to decreased immune system and organ function. This condition is assumed to be one of the factors for the emergence of pruritus in hemodialysis patients (Rroji, 2015). The results of Rroji's (2015) study stated that the elderly ( $\leq 72$  years and  $> 72$ ) complained more about pruritus because they experienced a downturn in the immune system. When the patient underwent hemodialysis there was a reaction on the skin and for a long time, the patient experienced dry and itchy skin (Weiss, 2015); (Ersoy, N. A., dan A. I., 2019) dan (Kaur, 2019). According to Weiss (2015), the distribution of pruritus is mostly complained of by patients aged 70-80 years. Age is a risk factor that cannot be controlled as a cause of disease. As we get older, the immune system is also indicated to have decreased, this causes people with older age to have a greater risk of developing pruritus symptoms.

## **V. CONCLUSION**

Thirteen articles were identified and analyzed, proving that uremic pruritus is a serious problem among hemodialysis patients. From the study summary, the results provide reliable evidence that the risk factors for uremic pruritus are multifactorial. Uremic pruritus arises because of risk factors for clinical value, adequate dialysis, length of time on dialysis, age, and sex. The clinical values referred to are urea, creatinine, hemoglobin, Urea Reduction Ratio, Clearance, Interleukin-2, Interleukin-6, and C-Reactive Protein.

It is necessary to do more research on the accuracy of hemodialysis dose because of the clinical parameters that can be excreted and the hemodialysis frequency.

This research is important because it is still unclear about how much hemodialysis frequency is sufficient and is still different. In accordance with the continuous kidney function, also the ideal frequency that must be applied.

Future research is also expected to be broader, including peritoneal dialysis patients, considering uremic pruritus is also a complaint by dialysis patients although the data shows that cases are higher in hemodialysis patients. A varied sample will be more representative and general. Maximum understanding of uremic pruritus factors is expected to improve management abilities, especially nursing care.

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