

Viral Hepatitis and Unexplained Itching in Chronic Hemodialysis Patients: Is There any Possible Association?

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Abstract

Back ground: Pruritus is commonly encountered in individuals with end-stage renal failure on dialysis. Various factors have been incriminated in the etiopathogenesis of pruritus, but its exact cause in this setting remains undetermined.

Aim: The aim of this study was to evaluate the possible correlation of viral hepatitis with both the prevalence and degree of pruritus in chronic hemodialysis (HD) patients.

Patients and Methods: Eighty four adequately dialyzed HD patients attending the HD unit of King Abdul-Aziz hospital, Holy Makkah, Saudi Arabia, were involved in this study. All the participants were subjected to complete history taking, thorough clinical examination, and routine

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laboratory investigations. Pruritus score (PS) was evaluated by means of a questionnaire and scored as follows: mild with PS of 1-7, moderate with PS of 8-14, and severe with PS of \geq or = 15.

Results: In this work, 62/84 patients (74%) were complaining of variable degrees of pruritus. The remaining 22/84 patients (26%) did not complain of pruritus and were considered as a control group. The hepatitis C virus antibody (HCV ab) (+ve) group comprised 69% (58/84); whereas hepatitis B surface antigen (HbsAg) (+ve) one involved 9.5% (8/84) of the patients having viral hepatitis, either pruritic or non-pruritic. Viral hepatitis, HCV and HBV, infection was found to be more prevalent in the studied HD patients with pruritus (81%) when compared to those having no viral hepatitis with pruritus (19%). The former value was significantly higher than that in non-pruritic HD patients with viral hepatitis (16/22, 73%) ($p < 0.05$). The PS was moderate to

severe in pruritic patients having viral hepatitis with the highest score was⁽¹⁹⁾. However, it was mild to moderate in pruritic patients having no viral hepatitis with the highest score was⁽¹³⁾. The difference between both groups was statistically significant ($p < 0.05$). The studied hematological and biochemical parameters showed neither significant differences between the studied groups nor significant correlations with PS. It can be concluded that a possible relationship exists between viral hepatitis and pruritus in HD patients.

Conclusions: Therefore, viral hepatitis screening is recommended for HD patients with unexplained intolerable pruritus.

Introduction

Pruritus is a disturbing epiphenomenon of uremia with unclear pathophysiology

mechanisms⁽¹⁾. Of all the systemic disorders, uremia is certainly the most important cause of pruritus and, among the dermatological abnormalities that can be associated with advanced chronic renal failure; pruritus is certainly the most disturbing disorder⁽²⁾.

The association between uremia and pruritus has already been reported more than a century ago⁽³⁾. The etiology is often multifactorial. Xerosis, hypercalcemia, hyperphosphatemia, hyperparathyroidism, and inadequate dialysis are among the causes⁽⁴⁾. Additionally, elevated plasma histamine levels and increased mast cell proliferation in the skin have been reported in patients⁽⁵⁾. Very few anecdotal reports suggesting an association between viral hepatitis infection and itching in dialysis patients are available in the literature^(6,7).

In this work, the possible association of viral hepatitis with the prevalence and degree of pruritus in chronic HD patients was studied.

Patients and Methods

Eighty four adequately dialyzed chronic patients attending the HD unit of King Abdul-Aziz hospital, Holy Makkah, Saudi Arabia, were involved in this study. All the participants were subjected to complete history taking, thorough clinical examination, and routine laboratory investigations. The latter involved complete blood picture, serum ferritin, renal function tests (blood urea and serum creatinine), liver function tests [aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (AP), serum bilirubin, and serum albumin], serum electrolytes

(sodium, potassium, calcium, and phosphorous), and parathormone (PTH). Hepatitis B surface antigen (HBsAg) and antibodies to HCV (HCV ab) were investigated using Enzygnost[®] HBsAg 5.0 (Dade Behring Inc., Marburg, Germany) and Innostest % HCV Ab IV ELISA 3rd generation (Innogenetics N.V., Ghent, Belgium), respectively.

In this study, 62/84 patients (74%) were complaining of variable degrees of pruritus. The remaining 22/84 patients (26%) did not complain of pruritus and were considered as a control group. Other causes of pruritus, such as primary pruritic skin disorders, drug reactions, obstructive biliary disease, endocrine disorders, hematological and solid malignancies, and neuropsychiatric disorders were excluded.

Pruritus score (PS) was evaluated by means of a questionnaire and scored as follows: mild with PS of 1-7, moderate with PS of 8-14, and severe with PS of \geq or = 15.

The distribution, frequency, severity of itching, and pruritus-related-sleep disturbance were assessed by means of a questionnaire and scored as follows⁽⁸⁾.

Distribution

Itching at one location received 1 point, more than two locations received 2 points, and generalized itching received 3 points.

Frequency

Episodic itching received 1 point, frequent itching received 2 points, and continuous itching received 3 points.

Severity

A slight itching sensation without necessity of scratching

received 1 point, with necessity to scratch, but without excoriations received 2 points, scratching accompanied by localized excoriations received 3 points. Pruritus associated with generalized excoriations leading to total restlessness received 5 points.

Sleep disturbance

A rare episode of waking up because of itching received 0 point, occasional itching leading to waking up received 2 points, frequent itching with subsequent waking up received 4 points, and lastly, itching resulting in total restlessness received 6 points.

Three pruritus grades were defined: mild with pruritus score (PS) of 1-7, moderate with PS of 8-14, and severe with PS of \geq or = 15.

The major limitation of the study is that any assessment based on subjective description will always have limitations of reproducibility. In pruritus, the severity may vary or may be fluctuating. Also, the patients have to recall the symptoms and site, particularly if the pruritus is not distressing to them. This leads to recall bias. To overcome this, pruritus was scored on at least two occasions with one week apart.

Results

In the studied HD patients, 62/84 patients (74%) were complaining of variable degrees of pruritus. The remaining 22/84 patients (26%) did not complain of pruritus (the control group). The HCV ab (+ve) group comprised 69% (58/84); whereas HBsAg (+ve) one involved 9.5% (8/84) of the patients having viral hepatitis, either pruritic or non-pruritic. Viral hepatitis, HCV and HBV, infection

was found to be more prevalent in the studied HD patients with pruritus (81%) when compared to those having no viral hepatitis with pruritus (19%). The former value was significantly higher than that in non-pruritic HD patients with viral hepatitis (16/22, 73%) ($p < 0.05$) (Table 1).

The PS was moderate to severe in pruritic patients having viral hepatitis (50/62, 81%) the highest score was 19. The mean \pm SD of PS in HCV ab (+ve) patients with pruritus (44/62, 71%) was 16 ± 3 . The PS in HBsAg (+ve) patients with pruritus (6/62, 9.7%) showed a mean \pm SD of 14 ± 2 . The difference in PS between HCV ab (+ve) and HBsAg (+ve) groups was statistically insignificant ($p > 0.05$). However, the difference in PS between both groups, with and without viral hepatitis, was statistically significant ($p < 0.05$) (Table 2).

The studied hematological and biochemical parameters showed neither significant differences between the studied groups nor significant correlations with PS (Table 1).

Discussion

Pruritus afflicts between 60% and 90% of dialysis patients. The temporal relationship between dialysis and pruritus is varied. The exact cause of pruritus in this setting remains undetermined, but several hypotheses abound^(9,10,11).

The studied hematological and biochemical parameters showed no significant differences between the studied groups or significant correlations with PS. These findings are in agreement with those of De Marchi et al⁽¹²⁾, Hiroshige et al⁽¹³⁾, and Mamianetti et al⁽¹⁴⁾, who reported absence of

any correlation between these parameters and pruritus.

In the present study, the levels of AST and ALT were not significantly higher in HD patients infected with viral hepatitis in comparison with those having no infection. This has been explained by the low baseline serum aminotransferase levels in dialysis patients. Therefore, the finding of a value slightly above the upper limits of normal or of a substantial rise within the normal range should be considered as an alarming sign for a possible underlying disease such as hepatitis⁽¹⁵⁾.

There is a well-recognized association between pruritus and chronic viral hepatitis infection⁽¹⁶⁾. It seems that chronic viral hepatitis infection with moderate to severe fibrosis may result in low-grade cholestasis with pruritus, possibly in association with bile duct disappearance as suggested by China et al⁽¹⁷⁾.

HD patients are at an increased risk of developing liver disease caused by blood-borne viruses. HCV infection is endemic among patients on dialysis^(18,19). This is probably related to the immunocompromised status of uremic patients, use of non-dedicated machines, previous blood transfusions, and nosocomial infection^(20,21). On the other hand, the incidence of hepatitis B infection, which is a significant cause of morbidity and mortality in HD patients, is fortunately on the decline in this patient population⁽²²⁾.

The incidence and prevalence of HCV infection among patients on dialysis, it varies widely in different countries^(23,24). In the United States the prevalence of HCV infection was 10.4% (range 0% to 64%) among patients from

different dialysis centers^(18,19). The prevalence varies in the other continents as well, ranging from 1-29% in Western Europe to 44-60% in the Far East⁽²⁵⁾. In the Arab World, the prevalence of HCV positivity in HD patients is quite different. It ranges from 26.5% in Oman to 80% in Egypt as reported by Barsom et al⁽²⁶⁾.

In the current study, the prevalence of HCV positivity among HD patients was 69%. This is consistent with the findings of Souqiyyeh et al⁽²⁷⁾, who reported that 70% of HD patients in Saudi Arabia were infected with HCV. However, the prevalence varies from one region to another where it was found to be 83.9% in the Central region, 94.7% in the Southern region, 15% in the Northern region⁽²⁸⁾, and 72.3% in the Western region⁽²⁹⁾.

In this work, pruritus was found to be more prevalent in the studied HD patients with viral hepatitis, HCV and HBV, infection (50/62, 81%) when compared to those having pruritus without viral hepatitis (12/62, 19.4%). The former value was significantly higher than that in non-pruritic HD patients with viral hepatitis which was 73% (16/22) ($p < 0.05$). The PS was moderate to severe in patients having viral hepatitis with the highest score being 19. However, it was mild to moderate in patients having no viral hepatitis with the highest score being 13. Statistically, the difference between both groups was significant ($p < 0.05$). These results were consistent with the findings of Hung et al⁽⁶⁾, and Hung et al⁽⁷⁾.

Conclusion

Viral hepatitis is a common disease with significant morbidity

and mortality. It is a known cause of acute and chronic liver disease in HD patients. Because the disease can be asymptomatic in its acute and chronic stages, the diagnosis is often missed. Intolerable pruritus may be a presenting symptom of viral hepatitis in HD patients.

From this study, it can be concluded that a possible relationship does exist between viral hepatitis and high grades of pruritus in HD patients. Therefore, screening of viral hepatitis infection is recommended for uremic patients on HD with unexplained intolerable pruritus.

Whether therapy directed to the incriminated viral infection is effective in controlling pruritus has to be studied. This is a single-center study with a limited number of patients and should be confirmed by other multicenter prospective trials with larger numbers of patients.

Table (1): The predialysis hematological, biochemical, and serological parameters in the studied group.

Parameters	Patients with pruritus n= 62 (74%)		Patients without pruritus n= 22 (26%)	
	With viral hepatitis n=50 (81%) Mean ± SD	Without viral hepatitis n=12 (19%) Mean ± SD	With viral hepatitis n=16 (73%) Mean ± SD	Without viral hepatitis n=6 (27%) Mean ± SD
WBC/L	5.3 x 10 ⁹ ±1.3	6.2 x 10 ⁹ ±1.4	5.3 x 10 ⁹ ±1.4	6.3 x 10 ⁹ ±1.3
Hb (gm/dl)	9.9±1.2	9.4±1.3	9.8±1.12	10.4±1.4
Platelets/L	153 x 10 ⁹ ±28.7	165 x 10 ⁹ ±22.7	156 x 10 ⁹ ±24.3	172 x 10 ⁹ ±33.5
Ferritin (ng/ml)	120±53.3	109±43.4	114±34.3	130±15.2
Blood urea (mg/ml)	174±43.6	168±45.7	162±39.4	171±38.5
Creatinine (mg/dl)	11.96±4.6	11.45±4.5	11.52±3.3	12±4.4
Kt/V*	1.2±0.34	1.2±0.31	1.1±0.12	1.2±0.23
AST (IU/L)	28±14.5	27±13.6	28±12.3	27±11.4
ALT (IU/L)	30±19.6	29±18.5	32±17.3	31±16.2
AP (IU/L)	110±30.4	107±27.1	97±14.7	95±13.3
Bilirubin (mg/dl)	1.6±0.5	0.9±0.2	1±0.3	0.7±0.2
Albumin (gm/dl)	2.8±0.7	3.1±0.9	2.9±0.6	3.3±0.8
Potassium (mmol/L)	5.6±0.8	5.4±1.5	4.5±1.2	5.3±0.7
Sodium (mg/dl)	141±4.5	138±3.6	136±5.3	140±4.7
Calcium (mg/ml)	6.8±1.5	6.2±1.8	7.1±1.3	6.9±1.2
Phosphorous (mg/dl)	3.4±1.8	3.5±1.7	3.3±1.5	3.4±1.3
PTH (pg/ml)	390±220.6	392±231.4	370±210.3	382±251.6
HBsAg (+ve)	6/62 (9.7%)	-	2/22 (9%)	-
HCV ab (+ve)	44/62 (71%)	-	14/22 (64%)	-

*Kt/V: Fractional clearance index for urea (K = total urea clearance, t = hemodialysis time in minutes, V = urea distribution volume).

Table (2): The mean±SD of pruritus score (PS) in the studied group.

	HD patients with pruritus n= 62/84 (74%)		
	with viral hepruritus 50/62 (81%)		Without viral hepruritus 12/62 (19%)
	HCV ab (+ve) 44/62 (71%)	HBsAg (+ve) 6/62 (9.7%)	
PS (mean±SD)	16 ± 3	14 ± 2	9 ± 4<None>

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