

**CHRONIC PRURITUS WITHOUT SKIN RASH– EVALUATION OF SYSTEMIC CAUSES**Amudha Renganathan<sup>1</sup>, Narmadha Selvaraj<sup>2</sup><sup>1</sup>Senior Assistant Professor, Department of Dermatovenereology, Trichy K.A.P.V. Government Medical College, Trichy.<sup>2</sup>Senior Assistant Professor, Department of Dermatovenereology, Trichy K.A.P.V. Government Medical College, Trichy.**ABSTRACT****BACKGROUND**

Pruritus lasting more than 6 weeks is termed chronic pruritus. Certain systemic diseases have long been known to cause pruritus that ranges in intensity from a mild annoyance to an intractable, disabling condition. Generalized pruritus may be classified into the following categories on the basis of the underlying causative diseases like renal pruritus, cholestatic pruritus, haematologic pruritus, endocrine pruritus, pruritus related to malignancy and idiopathic generalized pruritus.

The aim of this study was to evaluate the systemic causes of chronic pruritus without skin rashes.

**MATERIALS AND METHODS**

A descriptive cum analytical study was performed for a period of nine months duration.

Inclusion Criteria- Pruritus of more than six weeks duration without skin rash: female and male of any age group are included in this study. Exclusion Criteria- Patients with skin rashes are not included in this study. All patients were evaluated with history and complete physical examination. Blood investigations like complete blood count, blood sugar, renal function test, liver function test and peripheral smear study were done for all patients. Investigations for thyroid disorders and haematologic causes were done for required patients. USG abdomen and CT scan were also done for required patients. Expert's opinion obtained for those patients having psychological and neurological signs and symptoms.

**RESULTS**

For a period of nine months duration 100 patients were evaluated and tabulated. By this study, various systemic diseases were diagnosed and treated. For further evaluation and treatment certain patients were referred to other speciality departments. Limitations- A small number of patients during this period was a limiting factor.

**CONCLUSION**

By evaluating the systemic causes of chronic pruritus without skin rash, hidden cases can be brought out and it helps for the treatment purpose also.

**KEYWORDS**

Chronic Pruritus, Diabetes Mellitus, Aquagenic Pruritus, Psychogenic Itch, Systemic Diseases.

**HOW TO CITE THIS ARTICLE:** Renganathan A, Selvaraj N. Chronic pruritus without skin rash– evaluation of systemic causes. J. Evid. Based Med. Healthc. 2017; 4(19), 1076-1081. DOI: 10.18410/jebmh/2017/211

**BACKGROUND**

Chronic pruritus in the absence of a primary dermatologic etiology may be indicative of a serious underlying systemic diseases. Studies have shown that 14% to 24 % of patients presenting to a dermatologist's clinic with pruritus and no primary dermatologic cause have a systemic condition. The initial clinical approach in patients with chronic pruritus includes a complete history and thorough physical examination. Physical examination should include evaluation of liver, spleen and lymph nodes. Organomegaly increases the likelihood of an underlying systemic diseases such as

lymphoma. Chronic or generalised pruritus, age older than 65 years and abnormal physical findings should increase concern for an underlying systemic condition. In the absence of a primary skin lesion, the review of system should include evaluation for thyroid disorders, diabetes mellitus, kidney and liver diseases and lymphoma.<sup>1,2,3,4,5</sup>

Pruritus is one of the most troublesome symptoms seen in dermatologic practice. Severe pruritus can undoubtedly affect quality of life and can have serious psychological implication. Itching can be intractable and incapacitating as well as a diagnostic and therapeutic challenge. Satisfactory management of pruritus unassociated with any skin lesions still remains a distant goal.<sup>1,2,3,6,7,8</sup>

**MATERIALS AND METHODS**

100 patients with chronic pruritus and without skin manifestation were evaluated for systemic diseases. This study was done for a period of 9 months duration. Inclusion criteria includes both male and female of any age group with chronic pruritus and without any cutaneous manifestations. Exclusion criteria includes pruritus of less than 6 weeks

*Financial or Other, Competing Interest: None.*  
*Submission 22-01-2017, Peer Review 30-01-2017,*  
*Acceptance 13-02-2017, Published 03-03-2017.*

*Corresponding Author:*

Dr. Amudha Renganathan,  
MDDVI, 24- Muthu Avenue, 5<sup>th</sup> Cross,  
God's Park, 5<sup>th</sup> Main Road,  
Srinivasa Nagar, Trichy-620017, Tamil Nadu.  
E-mail: dramudha4@gmail.com  
DOI: 10.18410/jebmh/2017/211



duration and with skin rash. An informed consent was taken to each patient and then by descriptive cum analytical study all patients were evaluated that includes a complete history i.e., pruritus associated symptoms, complete physical examination including looking for organomegaly and lymph node enlargement.

Complete blood count, peripheral smear study, blood sugar, renal function test and liver function test were done for all patients. Procedures like x-ray chest, thyroid profile, USG abdomen and CT scan were done based on the

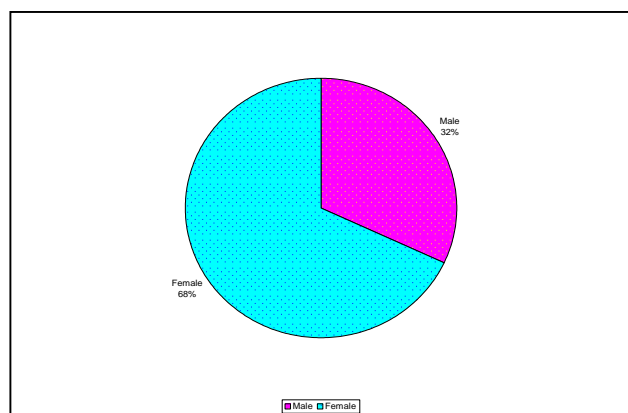
requirement of the patients. Opinions from experts especially from psychiatry and neurology department were considered for required patients.

## RESULTS

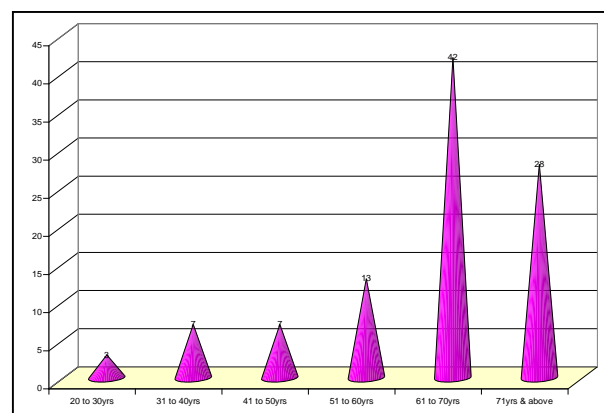
The relevant details are calculated and tabulated. The following table describes the prevalence of various category that includes sex incidence, age group, pruritus associated symptoms and systemic diseases evaluated by this study.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid		2	2.0	2.0	2.0
	Male	32	31.4	31.4	33.3
	Female	68	66.7	66.7	100.0
	<b>Total</b>	<b>102</b>	<b>100.0</b>	<b>100.0</b>	

**Table 1. Gender**



**Graph 1**



**Graph 2**

Particulars	Number of Respondents	Percentage
20 to 30 yrs.	3	3.0
31 to 40 yrs.	7	7.0
41 to 50 yrs.	7	7.0
51 to 60 yrs.	13	13.0
61 to 70 yrs.	42	42.0
71 yrs. & above	28	28.0
<b>Total</b>	<b>100</b>	<b>100</b>

**Table 2. Age**

No.	Signs & Symptoms	Number	Percentage
1	Loss of weight	7	7%
2	Weight Gain	2	2%
3	Constipation	3	3%
4	Frequency of stools	2	2%
5	Sleep disturbances	25	25%
6	Mood changes	10	10%
7	Tiredness	31	31%
8	Thyroid swelling	1	1%

**Table 3. Associated Signs and Symptoms**

		Sum of Squares	df	Mean Square	F	Sig.
age	Between Groups	31.353	11	2.850	2.979	.002
	Within Groups	84.207	89	.957		
	<b>Total</b>	<b>115.560</b>	<b>100</b>			
Durations	Between Groups	15.183	11	1.380	3.559	.000
	Within Groups	34.127	89	.388		
	<b>Total</b>	<b>49.310</b>	<b>100</b>			

**Table 4. ANOVA for Diagnosis**

Sl. No.	Name of the Diseases	No	%
1.	Diabetes Mellitus	18	18
	New Case	7	
	Old Case	11	
2.	Psychiatric Causes	11	11
	Depression	6	
	Anxiety Neurosis	3	
	Hypochondrial Disease with Anxiety	1	
	Obsessive – Compulsive Disorder	2	
3.	Thyroid Disorders	6	6
	Hyperthyroidism	2	
	Hypothyroidism	4	
4.	Iron Deficiency Anaemia	11	11
	With Systemic Diseases	3	
5.	Chronic Renal Diseases	3	3
	With Diabetes	1	
6.	Chronic Liver Disease	1	1
7.	Drug Induced Pruritus	1	1
8.	Liver Malignancy	1	1
9.	HIV	1	1
10.	Aquagenic Pruritus	1	1
11.	Senile Pruritus	34	34
12.	Idiopathic	12	12
<b>Table 5. Systemic Diseases</b>			

## DISCUSSION

This study was done for a period of 9 months duration. During the period of study, 118 patients came with complaints of chronic pruritus without skin rashes. Among them 18 patients were deleted from this study due to irregularity in their visit. Remaining 100 patients were evaluated for the underlying systemic causes.

In our study, we found that the prevalence of pruritus increased with age. The common age group with pruritus were between 61 to 70 years (42%). We also found that the majority of patients were women (68%). Both the above findings were comparable to most other studies. The prevalence of pruritus increases with age and can be partially attributed to a decline in the normal physiological status of the skin. In a study conducted in Norway, itching was the predominant skin complaint in subjects ranging from 30 to 76 years of age.<sup>9,10</sup> In a study by Beauregard and Gilcrest, two third of the geriatric patients reported pruritus as their major skin problem.<sup>9</sup> The prevalence of pruritus increased with age from 12.3% (16 to 30 years) to 20.3% (61 to 70 Years).<sup>11,12,13</sup>

Elderly people are believed to be particularly prone to chronic pruritus.<sup>14,15</sup> One population based study found a significant association between age and lifetime prevalence of chronic pruritus. Matteredne and colleagues study revealed the association of female gender with chronic pruritus; Women had more neuropathic and psychosomatic diseases underlying the chronic pruritus compared to men. (female – 54.8%).<sup>1,9,10</sup> According to a Turkish study, pruritus was the

common skin symptoms with 11.5% affected. Women were more affected (12.0%) than men (11.2%).<sup>13,16</sup>

In a view of our findings that the prevalence of systemic diseases were 54%. The prevalence of systemic diseases varied in different studies. Underlying systemic diseases were reported in 10 to 50% patients who seeks medical attention for pruritus.<sup>1</sup> A prospective study done showed that, of 55 patients 12 had a systemic cause of pruritus. A retrospective study done showed that 30% of cases to have systemic diseases.<sup>1,2,3,8,9</sup>

Generalized pruritus is attributed to systemic disease in 16% to 50% of individuals. One study reported that in 13.3% of the sample, pruritus is attributable for a single systemic cause, while in 24.7% a multifactorial causation was established.(Sommer et al.2007).<sup>17,18</sup>

According to our study, It has been found that the prevalence of diabetes mellitus was 18% that includes both old diabetic patients (11%) and newly diagnosed patients (7%). For those old diabetic patients, the diabetic status was not under control and few patients were having diabetes for long duration. In a study conducted, the generalized pruritus without skin manifestations was present in only 8 diabetic patients (2.7%).<sup>19</sup> Pruritus is often associated with diabetes mellitus although this is remaining controversial.<sup>20</sup>

As per Al-Mutairi et al study the prevalence of pruritus among diabetic patients was 49%. A study in elderly subject showed diabetes to be a statistically significant predictor of pruritus. In contrast, one study showed that generalized pruritus of unknown cause was especially common in patients with diabetes (8/300).<sup>20</sup> Ko et al studied the link between glycemic control and generalised pruritus in 385 patients with type 2 diabetes. A significant number of patients (27.5%) suffered from pruritus resulting in sleep disturbance.<sup>20</sup> Generalised pruritus was once considered a typical symptom of diabetes but its frequency is unknown. Studies have failed to provide a statistical basis for this belief.<sup>21</sup> Metabolic abnormalities, autonomic dysfunction, anhydrosis and diabetic neuropathy all may contribute to generalised pruritus.<sup>20</sup>

The prevalence of iron deficiency anaemia was 11% according to our study. In that 3% of patients were associated with systemic diseases like hypothyroidism, diabetes and chronic renal disease. Iron deficiency is often regarded as a cause of pruritus, even in the absence of anaemia, iron loading abolishes the symptoms. Pruritus is considered as one of the common manifestations of iron deficiency anaemia. Iron deficiency anaemia contributes to renal itch according to some authors. But they couldn't find any relationship between haematocrit level and uremic pruritus as shown in more recent studies.<sup>7,22</sup>

Our results suggest that the prevalence of thyroid diseases was 6% that includes both hyperthyroidism (1%) and hypothyroidism (5%). In our study patient with hyperthyroidism was suffering from pruritus without any cutaneous manifestations for the past 6 months duration, and she was having associated signs and symptoms like thyroid swelling, loss of weight and heat intolerance. In a Malaysian study of 236 patients with hyperthyroidism up to

6.4% patients had symptoms of pruritus, among them two third of cases were presented with pruritus alone.<sup>23</sup> Among the endocrine diseases thyrotoxicosis is associated with itching in upto 10% of patients especially with long standing disease. An increase in blood flow consequently in skin temperature may be a causative factor in hyperthyroidism.<sup>7,24</sup> According to a study the percentage of pruritus among hypothyroidism patients was 18%.<sup>33</sup> Common endocrine disorders associated with pruritus are hypothyroidism and hyperthyroidism.<sup>25,7</sup>

In this study we found that 11% of psychiatric patients were found to be suffering from chronic pruritus. The psychiatric diseases diagnosed by this study were depression, anxiety neurosis, hypochondrial disease with anxiety and obsessive-compulsive disorder. Among psychiatric inpatients, idiopathic itch was found to affect 36% to 42% of the patients, and was more frequent in those who exhibited anger-trait, angry temperament and ruminative catastrophization.<sup>8,26</sup> In a reference article patients with psychogenic itch predominantly were female. This finding correlates with our study bringing out the fact that the majority of psychiatric patients are found to be female. Of the chronic pruritus patients, 70.6% had psychiatric disorders ranging from one to three chronic pruritus can persist for months or even years, can reoccur after the termination of treatment.<sup>8,26,27,28</sup>

A large population – based cross - sectional study found a strong negative association between social support and severity of itch. The presence of idiopathic pruritus among psychiatric inpatient was also found to be associated with inadequacy of social support and unemployment. In our study also most of the patients lack social support from husband and relatives. Few patients lost their life partner in the early married life. According to a study, idiopathic pruritus was experienced by 42% of the subjects, 34% of the men and 58% of the women. The presence of idiopathic pruritus was found to be related to psychosocial stress with a prevalence of 48.5% among those without adequate social support and 29.5% among those with adequate social support.<sup>28</sup> Drug induced pruritus can be localised or generalised and may resolve shortly after drug discontinuation or may persist even for several months or years after treatment withdrawal. In a recent analysis of drug reactions, 12.5% showed pruritus without skin lesions.<sup>7,29</sup>

In our study, drug induced pruritus was noticed in a female patient on chloroquine therapy. Several studies have suggested that there could be heredo-familial factors influencing chloroquine induced pruritus. Study has shown that, 133 (40.20%) of 331 patients experienced itching to chloroquine. In a recent analysis of 200 patients with drug reaction, 12.5% showed pruritus without skin lesions. Number of reasons for drug induced pruritus have been postulated, including cholestatic liver injury, xerosis of the skin, deposits of drugs or their metabolites in the skin or neurological alterations. Often the underlying mechanisms are not known.<sup>7,29,30</sup>

We found a case of aquagenic pruritus in our study. After complete evaluation, other causes of aquagenic pruritus were excluded. The exact mechanism of the condition is unknown, though some studies have suggested that itching occurs in response to increased fibrinolytic activity in the skin. Later studies indicated that inappropriate activation of the sympathetic nervous system may play a part. In a study reported prevalence of aquagenic pruritus was 4.5%.<sup>31,32,33</sup>

Number of senile pruritus diagnosed in this study was 34%. There is no known cause for senile pruritus. Infact, a diagnosis of senile pruritus should only be made, once the other possible causes of a itchy skin without a rash has been excluded.<sup>34,35,36</sup> A Turkish study found that pruritus was the commonest skin symptom among elderly patients with 11.5% affected. In a study done at Uttarakhand the prevalence of senile pruritus was 9.0%. It is important to identify the patterns of geriatric skin disorders for effective delivery of health care services. The diagnosis of Willan's itch should be reserved for generalized pruritus in the absence of xerosis or other recognisable cause. The pathophysiology of this form of pruritus is poorly understood, but it is likely that age related changes of the skin, cutaneous nerves, and other parts of the nervous system play a major role.<sup>9,35,14,36,15</sup>

It has been observed that among 100 patients only one case with chronic liver disease was found who was a known alcoholic for the past five years. Liver function tests were abnormal. USG abdomen showed hepatomegaly. Intractable pruritus is reported to be the prevalent manifestation of liver diseases. Itching is a complication of liver disorders in particular, those characterized by cholestasis. Itching from liver disorders can appear before other signs and symptoms of cholestasis development. The prevalence of pruritus with primary biliary cirrhosis was 69% according to a survey. According to a retrospective study from a tertiary referral research institute in The United States, 5% of patients with chronic Hepatitis C were presented with pruritus. From a centre in Europe reporting that 40% of the patients with chronic pruritus from liver disease had chronic viral hepatitis C or B infection.<sup>7,37,38,39</sup>

In this study we found that the prevalence of chronic kidney disease was 3%. Among that one patient was presenting kidney disease as a complication of diabetes mellitus. In a study, 150 cases of chronic kidney disease were evaluated for skin diseases. The number of patients having pruritus (28%) in this study is similar to the study of Falodan O et al (26.7%). A significantly positive correlation was demonstrated between two methods for evaluating pruritus. Uremic pruritus was found in 40.8% of patients. 36.1% of patients reported pruritus to have been present in the past during the renal disease period. Pruritus is common disabling problem in patients with advanced end-stage renal disease. The data suggest that uremic pruritus tends to be prolonged, frequent and intense and it can impair the patient's quality of life including a negative effect on sleep and mood.<sup>40,41</sup>

In our study a male patient suffering from intractable itching was diagnosed with underlying HIV. The prevalence

of chronic itch among HIV patients was 45% according to a study. Because of the cross-sectional design, this study demonstrates an association between HIV and pruritus but cannot prove causation.<sup>42</sup>

Malignancy is frequently feared as the lurking aetiology of chronic pruritus and therefore a second - line works-up is recommended which often includes computed tomography imaging. Paraneoplastic pruritus has also been associated with solid tumours other than lymphoma which is very common association. Paraneoplastic itch occurs early during the natural process or even precedes the clinical evidence of the malignancy. Although generalised idiopathic pruritus has been often linked to internal malignancy, there are few studies that examine the presence of itch in malignancies. The severity of the itch can be mild to unbearable and it may precede other symptoms of malignancy up to several years. In our study, we diagnosed a case of hepatocellular carcinoma after several and repeated investigations.<sup>43,44</sup>

We couldn't find any cutaneous manifestations or systemic diseases for 12 patients, aged between 35 to 45 years (F-9, M-3). Those patients should be followed with periodic re-evaluation for later manifestations.

## CONCLUSION

This study describes the existence of chronic pruritus in different internal disorders. It is quite important that the reason of pruritus to be discovered, for the application of an adequate therapy.<sup>7</sup> Patients with chronic idiopathic pruritus should be followed with periodic reevaluation if the symptoms persists, because an underlying disorder can manifest later.<sup>2</sup>

## REFERENCES

- [1] Butler DF. Pruritus and systemic disease work up—updated. 2016. [emedicine.medscape.com/article/1098029](http://emedicine.medscape.com/article/1098029).
- [2] Taylor JS, Zirwas MJ. Cleveland Clinic Center for continuing education. 2010. [www.clevelandclinicmeded.com/medica](http://www.clevelandclinicmeded.com/medica).
- [3] Cassano N, Tessari G, Vena GA, et al. Chronic pruritus in the absence of specific skin diseases: an update on pathophysiology, diagnosis and therapy. *Am J Clin Dermatol* 2010;11(6):399-411.
- [4] Reamy BV, Bunt CW, Fletcher S. A diagnostic approach to pruritus. *American Family Physician* 2011;84(2):195-202.
- [5] Wolff K, Johnson RA, Saavedra AP. Generalized pruritus without skin lesions (pruritus sine materia). In: Fitzpatrick's color atlas and synopsis of clinical dermatology. 7<sup>th</sup> edn. New York: McGraw-Hill 2005.
- [6] Moses S. Pruritus. *American Family Physician* 2003;68(6):1135-1142.
- [7] Yonova D. Pruritus in certain internal diseases. *Hippokratia* 2007;11(2):67-71.
- [8] Polat M, Oztas P, Ilhan MN, et al. Generalized pruritus: a prospective study concerning etiology. *Am J Clin Dermatol* 2008;9(1):39-44.
- [9] Cohen KR, Frank J, Salbu RL, et al. Pruritus in the elderly: clinical approaches to the improvement of quality of life. *PT* 2012;37(4):227-239.
- [10] EDF, European Academy of Dermatology and Venereology. European guideline on chronic pruritus. *Acta Derm Venereol* 2012;92:563-581.
- [11] Khan S, Healy R, Sahota A. Management of pruritus in the elderly. *MIMS Dermatology* 2013;8(4):29-32.
- [12] Stander S. Prevalence of chronic pruritus in Germany: results of a cross-sectional study in a sample working population of 11730. *Dermatology* 2010;221(3):229-235.
- [13] Grundmann S, Stander S. Chronic pruritus: clinics and treatment. *Ann Dermatol* 2011;23(1):1-11.
- [14] Jindal R, Jain A, Roy S, et al. Skin disorder among geriatric population at a tertiary care centre in Uttarakhand. *Dermatology section* 2016;10(03):WC06-WC08.
- [15] Ayer J. Itching in old age. *Dermatological Nursing* 2009;8(3):16-18.
- [16] Ständer S, Stumpf A, Osada N, et al. Gender differences in chronic pruritus: women present different morbidity, more scratch lesions and higher burden. *British Journal of Dermatology* 2013;168(6):1273-1280.
- [17] Weisshaar E, Mattered U. Epidemiology of itch. Chapter 2. In: Carstens E, Akiyama T, eds. *Itch: mechanisms and treatment*. Boca Raton (FL): CRC Press/Taylor & Francis 2014.
- [18] Khopkar U, Pande S. Etiopathogenesis of pruritus due to systemic causes: implication for treatment. *Indian J Dermatol Venereol Leprol* 2007;73(4):215-217.
- [19] Neilly JB, Martin A, Simpson N, et al. Pruritus in diabetes mellitus: investigation of prevalence and correlation with diabetes control. *Diabetes Care* 1986;9(3):273-275.
- [20] Babakinejad P, Walton S. Diabetes and pruritus. *The British Journal of Diabetes* 2016;16(4).
- [21] Jamwal A, Rather PA, Sharma A, et al. Cutaneous manifestations of hypothyroidism-prospective hospital based clinical study. *J Adv Med Dent Scie* 2013;1(2):5-12.
- [22] Nagan V. Iron deficiency. *Derm Net New Zealand* 2016.
- [23] Tan CE, Loh KY. Generalized pruritus as a presentation of Grave's disease. *Malaysian Family Physician* 2013;8(1):20-23.
- [24] Tivoli YA, Rubenstein RM. Pruritus. An updated look at an old problem. *J Clin Aesthet Dermatol* 2009;2(7):30-36.
- [25] Keen MA, Hassan I, Bhat MH. A clinical study of the cutaneous manifestations of hypothyroidism. *Indian J Dermatol* 2013;58(4):326.
- [26] Tey HL, Wallengren J, Yosipovitch G. Psychosomatic factors in pruritus. *Clin Dermatol* 2013;31(1):31-40.
- [27] Jain S. Problematic pruritus: seeking a cure for psychogenic itch. *Current Psychiatry* 2013;12(10):55.

- [28] Kretzmer GE, Gelkopt M, Kretzmer G, et al. Idiopathic pruritus in psychiatric in patients: an explorative study. *Gen Hosp Psychiatry* 2008;30(4):344-348.
- [29] Reich A, Ständer S, Szepietowski JC. Drug induced pruritus: a review. *Acta Derm Venereol* 2009;89(3):236-244.
- [30] Aghahowa SE, Obianwu HO, Isah AO, et al. Chloroquine- induced pruritus. *Indian J Pharm Sci* 2010;72(3):283-289.
- [31] Aquagenicpruritus.  
[https://en.wikipedia.org/wiki/Aquagenic\\_pruritus](https://en.wikipedia.org/wiki/Aquagenic_pruritus)
- [32] Salami TA, Samuel SO, Momoh MO. Prevalence and characteristics of aquagenic pruritus in a young African population. *BMC Dermatol* 2009;9:4.
- [33] Potasman I, Heinrich I, Bassan HM. Aquagenic pruritus: prevalence and characteristics. *Isr J Med Sci* 1990;26(9):499-503.
- [34] Itch skin without rash causes and senile pruritus in the elderly. 2012. [www.seniorhealth365.com](http://www.seniorhealth365.com)
- [35] Patange VS, Fernandez RJ. A study of geriatric dermatoses. *Indian J Dermatol Venereol Leprol* 1995;61(4):206-208.
- [36] Ward JR, Bernhard JD. Willan's itch and other causes of pruritus in the elderly. *International Journal of Dermatology* 2005;44(4):267-273.
- [37] Bergasa NV. Pruritus of cholestasis. Chapter 6. In: Carstens E, Akiyama T, eds. *Itch: mechanisms and treatment*. Boca Raton, FL: CRC Press/Taylor & Francis 2014.
- [38] Jamwal A, Rather PA, Sharma A, et al. Cutaneous manifestations of hypothyroidism-prospective hospital based clinical study. *J Adv Med Dent Scie* 2013;1(2):5-12.
- [39] Fred Schubert. Itchy skin and liver problems. 2015. <http://www.livestrong.com>
- [40] Gunipudi SK, Srirama S, Siddabathuni N, et al. A clinical study of cutaneous manifestations in patients with chronic kidney diseases. *IOSR* 2015;14(10):7-17.
- [41] Szepietowski JC, Sikora M, Kuzstal M, et al. Uremic pruritus: a clinical study of maintenance hemodialysis patients. *J Dermatol* 2002;29(10):621-627.
- [42] Kaushik SB, Cerci FB, Miracle J, et al. Chronic pruritus in HIV- positive patients in the south-eastern United States: its prevalence and effect on quality of life. *J Am Acad Dermatol* 2014;70(4):659-664.
- [43] Chan B. Paraneoplastic pruritus. *Derm Net NZ* 2014.
- [44] Fett N, Haynes K, Probert KJ, et al. 5 Year malignancy incidence in chronic pruritus patients: a-population-based cohort study. *J Am Acad Dermatol* 2014;70(4):651-658.