



# Association of Systemic Diseases with Chronic Pruritus

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## Abstract

**Background/Aim:** Pruritus is an unpleasant sensation that provokes the desire to scratch. It is one of the most common reasons why patients consult a dermatologist. Aim of this study was to determine the association of chronic pruritus with skin and systemic diseases, as well as the age and sex distribution in the studied population.

**Methods:** The cross-sectional study included 120 patients of both sexes who, in the period from January 2017 to January 2021, received outpatient and inpatient treatment at the Skin and Venereal Diseases Clinic of the University Clinical Centre of the Republic of Srpska diagnosed with pruritus. Through the Clinical Information System insight was gained into the medical history and other documentation of the subjects from which data were taken on the age and sex of the subjects, onset, course and duration of pruritus, daily or seasonal variations in intensity, as well as the presence of associated skin and systemic diseases.

**Results:** Out of a total of 120 subjects, a larger number (53.3 %) of subjects with chronic pruritus were male, and 46.7 % were female, the difference was statistically significant ( $p < 0.05$ ). The analysis of the distribution of subjects according to their age revealed that the largest number of subjects (62.6 %) was over 65 years of age, while 38.4 % of subjects were under 65 years of age. The difference in the age structure was statistically significant ( $p < 0.05$ ). In subjects older than 65 years pruritus was most frequently (47.3 %) associated with diabetes and in subjects under 65 years of age with skin diseases and conditions. The difference was statistically significant ( $p < 0.05$ ).

**Conclusion:** In people aged over 65 years, pruritus was most frequently associated with systemic diseases (diabetes mellitus) and in people aged under 65 years with dermatological diseases (*Dermatitis atopica*).

**Key words:** Chronic pruritus; Diabetes mellitus; Senile pruritus.

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## Introduction

Pruritus or itching is defined as an unpleasant sensation that provokes the desire to scratch.<sup>1</sup> It is one of the most common conditions, ie symptoms causing patients to consult a dermatologist. It is a symptom not only of many skin diseases but also systemic ones. Due to its diversity both in the clinical picture and etiopathogenesis, the treatment of pruritus can be a challenge. It is equally present in all races as well as in both

sexes.<sup>2</sup> It can be constantly present or intermittent and localised or generalised. Pruritus present for more than 6 weeks is defined as chronic one.<sup>3</sup> In addition to pruritus caused by skin disorders, it can also be distinguished systemic, neuropathic, psychogenic, multifactorial and idiopathic one.<sup>1</sup>

Skin disorders that cause pruritus mostly include dry skin, inflammatory dermatoses (primarily

atopic dermatitis), then infectious dermatoses, as well as cutaneous types of lymphoma.<sup>4, 5</sup> Systemic pruritus occurs as a result of diseases of other organs, most frequently the liver, kidneys, endocrine and haematological disorders, tumours, infectious conditions, as well as the use of certain drugs (antihypertensives, antiarrhythmics, anticoagulants, antidiabetics, antiepileptics, cytostatics and chemotherapeutics). Neuropathic pruritus occurs as a result of damage to the nerves or the use of opioids (neurogenic pruritus), while psychogenic pruritus, which is also called somatomorphic is accompanied by numerous psychiatric conditions. Due to the large number of chronic diseases and polymedication, there is a high incidence of pruritus among the elderly population.<sup>6, 7</sup> That is why the term senile pruritus is introduced, which means the presence of chronic pruritus of unknown cause in people aged over 65. In the elderly population, three possible reasons for the occurrence of pruritus have been described, namely dry skin, immunological and neuropathic cutaneous changes.<sup>8</sup> Given that the sensation and intensity of pruritus is subjective, a thorough anamnesis and dermatological examination are required for the diagnosis and successful treatment.

Clinical presentation is of great importance for the diagnosis of chronic pruritus. It can appear on clinically unchanged skin or be accompanied by various primary or secondary skin changes. Primary efflorescence can be a part of the clinical picture of the basis of the skin disease that caused pruritus, while secondary changes are the result of scratching (excoriations, crusts, lichenification, hyperpigmentation and hypopigmentation).<sup>9</sup> There are still many unknowns about the mechanisms of occurrence of chronic pruritus, but it is certain that it arises due to a complex interaction between keratinocytes, nerve fibres located in the dermis, prurigenic molecules and the central and peripheral nervous system.<sup>10</sup>

The aim of this research was to determine the association of chronic pruritus with skin and systemic diseases, as well as the age and sex distribution in the study population.

## Methods

The cross-sectional study included 120 patients of both sexes who were treated at the Skin and

Venereal Diseases Clinic of the University Clinical Centre of the Republic of the Srpska diagnosed with pruritus in the period from January 2017 to January 2021. Outpatients and inpatients in the specified period were included. Through the Clinical Information System insight was gained into the medical history and other documentation of the subjects from which data were taken on the age and sex of the subjects, onset, course and duration of pruritus, daily or seasonal variations in intensity, as well as the presence of associated skin and systemic diseases.

The study included subjects of both sexes aged over 18 years, in whom pruritus was present for more than six weeks. Patients in whom scabies was the cause of pruritus were not included because the duration of the disease is usually less than 6 weeks and as such it is not included within the framework of chronic pruritus. All subjects were divided into two groups. The first group consisted of patients aged up to 65 years and the second group consisted of patients aged over 65 years.

Statistical analysis of the collected data was done in the statistical software package of EZR for Windows XP (Version 2.3-0). Descriptive statistics were used to arrange and describe the data and they included the calculation of incidence. Chi-square test was used to compare the frequency of occurrence of the analysed categorical characteristics of one or more independent samples. All results were considered statistically significant if  $p < 0.05$  and highly statistically significant if  $p < 0.001$ . In the examples where highly statistically significant results were obtained, the level of statistical significance was written.

## Results

The study included a total of 120 subjects, 53.3 % of men and 46.7 % of women, who in a three-year period (from 1st January 2017 to 1st January 2021) were diagnosed with pruritus and treated at the Skin and Venereal Diseases Clinic of the University Clinical Centre of the Republic of the Srpska. The analysis of the distribution of subjects according to age revealed that 46 (38.4 %) subjects were aged under 65 years and 74 (61.6 %) were aged over 65 years. The analysis of the distribution of

subjects according to sex revealed that chronic pruritus was more frequently registered in male subjects aged over 65 years. The difference was statistically significant  $p < 0.05$  (Table 1).

**Table 1:** Distribution of chronic pruritus by age and gender

Gender	All patients		Age				p-value
	n	%	< 65		≥ 65		
Male	64	53.3	18	39.1	46	62.2	0.02*
Female	56	46.7	28	60.9	28	37.8	
Total	120	100.0	46	100.0	74	100.0	

\*The p-value refer to the Chi-square test.

Dermatological diseases, atopic dermatitis and dry skin were the most common causes of pruritus in the group of subjects aged under 65 years, while systemic diseases were the most common cause in subjects aged over 65 years. Dry skin was present in 30.4 % of subjects from this group and atopic dermatitis in 21.7 % of subjects. The most common systemic diseases that caused pruritus in the population of subjects over 65 years of age were diabetes mellitus (33.8 %) and malignancies, prostate and lung cancer in men and breast cancer in women. *Mycosis fungoides* was found in two subjects from this group. Malignant diseases as a cause of pruritus were also found in the subjects from the first group (carcinoma of the breast, colon and liver) in 13.2 % of the cases. Psychogenic pruritus was present in 4 (8.7 %) of the subjects under 65 years of age and in 16 (21.6 %) of the subjects over 65 years of age, more frequently women. Chronic pruritus, of unknown cause, was recorded in 8.3 % of all subjects, mostly without skin changes (Table 2).

**Table 2:** The most common causes of pruritus

Variable	All patients		Age				p-value
	n	%	< 65		≥ 65		
Skin diseases	37	30.8	24	38.7	13	17.6	0.001*
Systemic diseases	53	44.0	12	39.2	35	47.3	
Psychogenic	20	6.7	4	8.7	16	21.6	
Idiopathic	10	8.3	0	0	10	13.5	
Total	120	100.0	46	100.0	74	100.0	

\* The p-value refer to the Fisher exact test.

Within the clinical manifestations that appeared with pruritus, primary skin changes were analysed, as well as secondary ones that occurred as a result of scratching (Table 3). In 67.9 % of the subjects of both age groups pruritus was accompanied by certain skin changes. As for the primary skin manifestations, erythema, which was described as dull and maculopapular

rash, occurred most frequently. Analysis of the obtained data revealed that in all patients with malignant diseases, pruritus was accompanied by a maculopapular rash. Excoriations were present in 35 % of subjects. In all patients diagnosed with psychogenic pruritus (16.7 %) excoriations were the only clinical manifestation. There was 34.1 % of subjects without skin changes and it was determined that there was no statistical significance (Table 3).

**Table 3:** Correlation chronic pruritus and skin manifestations

Variable	All patients		Age				p-value
	n	%	< 65		≥ 65		
With skin manifestations	79	65.9	26	56.5	53	71.6	0.114*
Without skin manifestations	41	34.1	20	43.5	21	28.4	
Total	120	100.0	46	100.0	74	100.0	

\* The p-value refer to the Fisher exact test.

Seasonal variations in the intensity of pruritus were recorded in two subjects over 65 years of age, in whom pruritus lasted longer than 3 years. The subjective feeling was more pronounced in the winter months. When it comes to diurnal variations, a small number of subjects declared that they were more pronounced in the evening and night hours and this mostly relates to the women under 65 years of age, while the other subjects declared that there was no difference in the intensity of itching during the day.

## Discussion

Pruritus is one of the most common conditions and/or symptoms for which patients consult a dermatologist and the reason for about 10 % of all visits to a dermatologist.<sup>11</sup> The problem of pruritus is not exclusively related to the field of dermatology, but it is also dealt with by doctors of various other specialties. In this paper, the incidence of pruritus among dermatological patients of different age groups and its association with systemic diseases was analysed.

The results of the studies that dealt with the sex distribution of pruritus were not harmonised. However, authors would single out the research of Dalgard and al who, based on a sample of about 18,000 subjects concluded that pruritus was the most common dermatological condition in the study population and that it occurred more often in women.<sup>12</sup> In presented research on a smaller

number of subjects it was found that the incidence of pruritus was higher in men.

The results of this study showed that the incidence of pruritus was significantly higher in patients older than 65 years (62.2 %) and that it was most frequently associated with various systemic diseases (44.0 %), followed by dermatological diseases and conditions (the most common of which was dry skin) and psychogenic diseases (30.8 % and 16.75 %, respectively). In the smallest number of patients (8.3 %) the cause of pruritus was not determined. The association between pruritus and systemic diseases can be explained by the more frequent presence of not only various systemic diseases in old age, but also due to the physiological process of skin aging that leads to the development of senile pruritus, as well as the more frequent use of diuretics. Diabetes mellitus was the main cause of the development of chronic pruritus in the study population and it was registered in 24.2 % of the subjects, which was in correlation with similar studies.<sup>13, 14</sup> In the majority of patients with diabetes skin manifestations were in the form of erythema and papular rash, accompanied by excoriations. Diabetes mellitus, in addition to affecting blood vessels, has a major impact on all skin structures. Preclinical studies on animal models and a small number of clinical studies on patients have proven that diabetes mellitus leads to disorders in the architecture of the skin. It is the cause of a damaged skin barrier, increases inflammatory infiltration, reduces the number of T lymphocytes, antimicrobial peptides, lamellar bodies, lipids of the corneal layer as well as the proliferation of keratinocytes. It also reduces skin hydration and leads to alteration of filaggrins.<sup>15, 16</sup> Filaggrins are structural proteins of the corneal layer that cross-link keratin filaments and are crucial for maintaining the structure and function of the corneal layer and therefore, are necessary for maintaining skin hydration.<sup>17</sup>

Apart from diabetes, numerous studies point out that kidney failure is one of the most common causes of systemic pruritus and that pruritus is present in 60-80 % of patients with chronic renal failure.<sup>18-19</sup> However, in presented study, that number was significantly lower and was found in only 1.7 % of patients older than 65 years. The result of this disproportion may be the fact that patients with chronic renal failure are under the regular supervision of nephrologists who treat pruritus in a consultation with dermatologists.

In the population under the age of 65, pruritus was more frequently registered (38.7 %) in people with some skin diseases. Atopic dermatitis represents one of the most common dermatoses associated with pruritus and in addition to it, it is also found in dry skin. Presented results are correlated with data from the literature in which atopic dermatitis is one of the most pruriginous dermatoses, in which pruritus occurs in 87-100 % of patients.<sup>20</sup> In presented research, it was found that pruritus associated with dry skin occurred in 10 % of women under the age of 65, while in some studies the cause is significantly higher (up to 69 %).<sup>21</sup> Although dry skin is the cause of pruritus in 50 % of cases in the elderly population in the world,<sup>22</sup> in this study the number was significantly lower and it was 17.6 %. Dry skin does not have its primary efflorescence, but in these patients excoriations and lichenification could mostly be seen as a result of scratching. In addition to genetics, the basis of dry skin is an impaired function of the skin barrier, which in the younger female population can be explained by the irrational use of various cosmetic preparations not adapted to the skin type.

Data on the incidence of psychogenic pruritus are scarce because it is difficult to draw a clear line between psychogenic and idiopathic pruritus.<sup>23, 24</sup> Psychogenic pruritus was confirmed in 16.7 % of the study population, of which 8.3 % was the female population over the age of 65, but there was a possibility that in some patients with idiopathic pruritus it was actually psychogenic one. Excoriations were dominant skin changes present in these patients.

In the population of subjects over 65 years of age, apart from the expressed subjective feeling of itching, which was registered in a large number of subjects (71.6 %), there were also skin manifestations, most frequently expressed in the form of erythema, maculopapular rash and excoriations. Moreover, in the group of subjects under 65 years of age cutaneous manifestations were present in a larger number of subjects (56.5 %) while 43.5 % of subjects from this group were without skin changes.

Given that pruritus is an exclusively subjective symptom, it is very difficult to assess its intensity. Diurnal and seasonal variations are described. Diurnal variations, more pronounced in the evening hours, are associated with psychogenic pruritus and this was also recorded in studied

subjects. In this research reliable data on seasonal variations of pruritus could not be provided because the disease lasted longer than a year in a small number of subjects. However, it can be said that pruritus is more pronounced in the winter months in patients with atopic dermatitis and dry skin and this is most likely the result of excessive warming, wearing clothes made of synthetic materials as well as staying in closed rooms for a long time.

## Conclusion

Chronic pruritus is a problem that affects a large number of people of different ages and significantly reduces their quality of life. The results of presented study have shown that systemic diseases are the most common cause of chronic pruritus in the study population. Given that the aetiology of chronic pruritus is diverse, discovering the cause of its occurrence is a condition for successful treatment.

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## Conflict of interest

None.

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