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Sadržaj / Table of Contents

Comorbidity in women with psoriasis

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Abstract

Background: Psoriasis is a chronic disease, and patients develop associated diseases including obesity, dyslipidemia, high blood pressure, diabetes. Aim of the research: To determine the frequency of comorbidities (obesity, dyslipidemia, diabetes, high blood pressure) in women with psoriasis, and the influence of psoriasis severity on the occurrence of comorbidities.

Respondents and methods: A prospective study was conducted and included 85 women with psoriasis, mean age 50,26 years (SD=± 14,33), average duration of psoriasis 14,57 years (SD=± 11,78).

Results: 65,88% of psoriasis patients had associated diseases in this study. 50,59% had high blood pressure, 38,82% were obese, 30,59% had dyslipidemia, and 17,65% had diabetes. and PASI values were 11,30 (SD=± 6,40). There was a correlation between the severity of psoriasis, that is PASI score and high blood pressure (r=0,68), while there was no correlation between PASI score and obesity (r=0,38), dyslipidemia (r=0,33) and diabetes. 0,23.

Conclusion: Given the frequency of comorbidities, and even the occurrence of more of them in women with psoriasis, their detection and treatment are essential for the comprehensive treatment of psoriasis patients.

Key words: psoriasis, women, PASI score, comorbidities.

Introduction

Psoriasis is a chronic, inflammatory, multifactorial disease (Raho et al., 2012). It has been known since ancient times, and in recent times the occurrence of associated diseases has been frequently investigated. Thus, research has shown more frequent occurrence of high blood pressure, dyslipidemia, obesity, diabetes in patients with psoriasis (Duarte et al., 2016, Armstrong et al., 2012). Despite the more frequent occurrence of some diseases in patients with psoriasis, the mechanism of association between psoriasis and associated diseases has not been elucidated. Genetic, inflammatory and environmental factors are thought to influence the occurrence of associated diseases (Carvalho et al., 2016). Timely detection and treatment of associated diseases is very important. Because in Europe, 27,7% of patients with psoriasis with high blood pressure and 44,2% with dyslipidemia did not receive appropriate therapy (Ahlehoff et al., 2012). The prevalence or severity of psoriasis can vary. Studies show that the severity of psoriasis can affect the occurrence of comorbidities, patients with severe psoriasis compared to those with mild forms of the disease have shown a higher chance of developing comorbidities (Love et al., 2011, Azfar et Gelfand 2008).

AIM

To determine the frequency of comorbidities (obesity, dyslipidemia, diabetes, high blood pressure) in women with psoriasis, and the influence of psoriasis severity on the occurrence of comorbidities.

Respodents and methods

A prospective study was conducted that included 85 women with psoriasis over the age of 18. The mean age was 50,26 years (SD=± 14,33). The average duration of psoriasis was 14,57 years (SD=± 11,78), years. The most common form of psoriasis was psoriasis vulgaris in 85,88% of subjects, followed by psoriasis guttata and psoriasis pustulosa generalisata in 5,88% of subjects, and psoriasis pustulosa palmaris et plantaris in 2,35% of subjects.

The purpose and manner of conducting the research were explained, written consent to participate in the research was signed. The study involved women with psoriasis older than 18 years. Excluded from the study are women who, in addition to psoriasis, also suffer from some other skin disease, who have been suffering from psoriasis

for less than a year, who use systemic therapy for psoriasis, and pregnant and postpartum women.

The anamnesis was taken, a dermatological examination of the skin and visible mucous membranes was performed, after which they were subjected to research. All subjects were given a PASI score, BMI, fat and blood sugar values, and internists were referred for examination to diagnose obesity, high blood pressure, diabetes and dyslipidemia. For determining the severity and outspread of psoriasis, Psoriasis Area and Severity Index (PASI) was used. In four regions body-head, torso, upper and lower extremities. In the four regions of the body-head, torso, upper and lower extremities evaluated the characteristics of the disease, severity of erythema, infiltration and desquamation with the score 1-4, and the affected area of skin psoriatic changes with the score 1-6 (Table 1.). In assessing the severity of erythema scales may not be removed. Theoretically PASI can range from 0-72 (Frederiksson et Petersson 1978).

By this method we calculate:

- Buttocks as a part of lower extremities, that is, region of the leg (l)
- Armpits and shoulders as a part of upper extremities, that is, region of the arm (a)
- The neck is calculated as a part of the head (h)
- Torso (t)

For calculating the PASI, the summation of Erythemas, infiltrations and desquamations of single region is multiplied with the numerical value of the region of the body and with the percentage by which the lesions have spread at a single region. Results obtained for each single region are calculated in PASI.

Form for calculating PASI:

PASI=0,1x(Eh+Ih+Dh)xAh+0,3x(Et+It+Dt)xAt+0,2x(Ea+Ia+Da)xAa+0,4x(El+Il+Dl)xAl

Legend:

E- Erythema A – Area a - arm
I – Infiltration h – head l - leg
D – Desqumation t - torso

Determination of body mass index (BMI)

Body weight (expressed in kg) and body height (expressed in cm) were measured.

Body mass index was calculated by the formula: body weight in kg divided by body height expressed in meters squared

BMI = body weight (kg)/body height $(m)^2$

The reference values are:

- malnutrition, BMI lower 18,5 kg/m^2
- normal body weight, BMI 18,5-24,9 kg/m^2
- overweight, BMI 25,0 to 29,9 kg/m^2
- obesity, BMI greater than 30 kg/m^2
- obesity class I, BMI 30,0-34,9 kg/m^2
- obesity class II, BMI 35,0-39,9 kg/m^2
- Class III obesity (morbid obesity), BMI higher 40,0 kg/m^2

Blood sugar and fat values were measured by standard biochemical procedures, after taking a venous blood sample from subjects who had not eaten for at least 8 hours.

Reference values for lipids are: cholesterol ≤ 5.2 mmol/l, triglycerides ≤ 1.7 mmol/l.,

Glucose reference values are: ≤ 5.6 mmol/l.

Reference values of blood pressure are: <130 85mmHg.

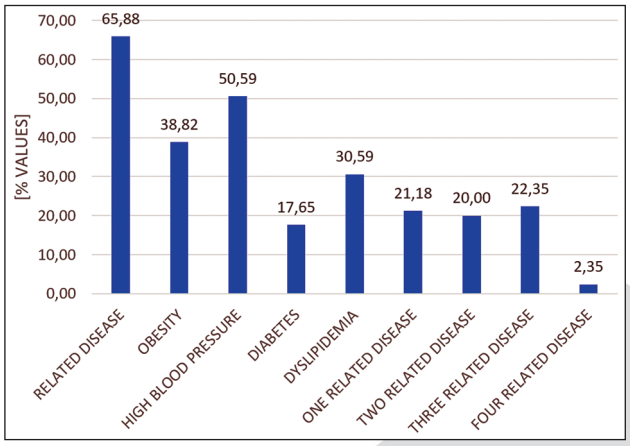
Statistical methods

For statistical data processing and obtaining results, the data were processed in Microsoft Excel. Intergroup differences were determined by the mean value with standard deviation. The Pearson correlation coefficient was used to assess the correlation of variables or correlations. The lowest value of the significance level is p <0,05.

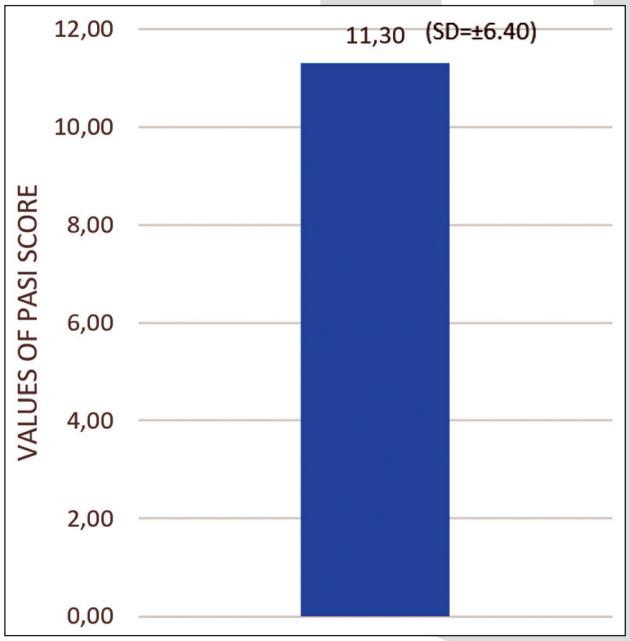
Table 1. Measurement of PASI

Grade	0	1	2	3	4	5	6
Erythema (E)	None	Mild	Medium	Strong	Very Strong	-	-
Infiltration (I)							
Desquamation (D)							
Enveloped area of the skin % (A)	0	1-9	10-29	30-49	50-69	70-89	90-100

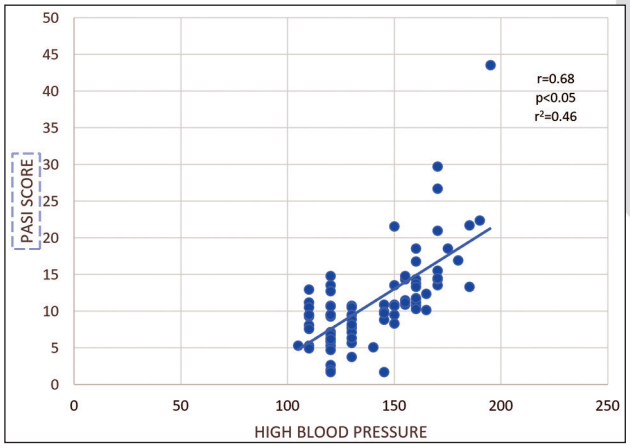
Results



Graph 1. Frequency of comorbidities in women with psoriasis

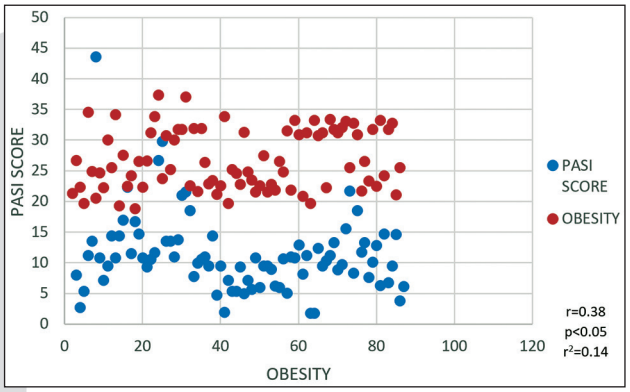


Graph 2. Values of PASI score



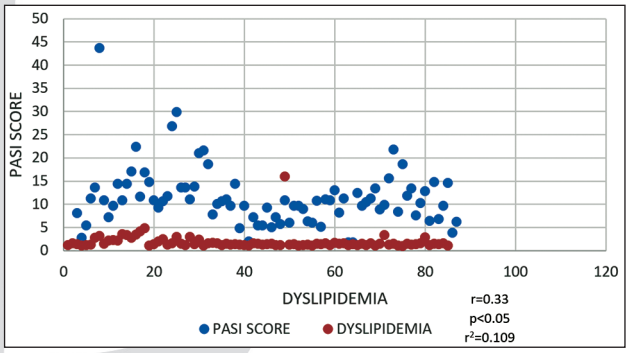
Graph 3. Correlation of PASI score and high blood pressure

The value of the correlation coefficient, ie the product-moment weight coefficient of the PASI score and elevated blood pressure is r=0,68, which indicates a medium strong correlation, and when we talk about the strength of the connection, it indicates a medium strong connection of these two variables.



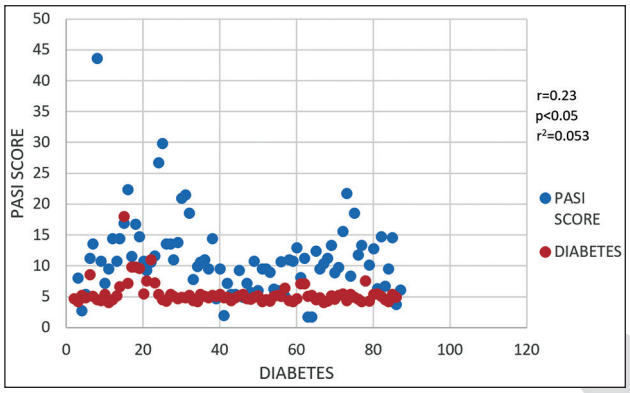
Graph 4. Correlation of PASI score and obesity

The value of the correlation coefficient, ie product-moment weight coefficient of PASI score and obesity is r=0,38, which indicates a relatively weak correlation, and when we talk about the strength of the connection, it indicates a weak connection between these two variables.



Graph 5. Correlation of PASI score and dyslipidemia

The value of the correlation coefficient, ie product-moment weight coefficient of PASI score and dyslipidemia is r=0,33, which indicates a relatively weak correlation, and when we talk about the strength of the connection, it indicates a weak connection between these two variables.



Graph 6. Correlation of PASI score and diabetes

The value of the correlation coefficient, ie the product-moment weight coefficient of the PASI score and diabetes is r=0,23, which indicates a relatively weak correlation, and when we talk about the strength of the connection, it indicates a weak connection between these two variables.

Discussion

A study was conducted to determine the occurrence and frequency of comorbidities in women with psoriasis, and to assess the impact of psoriasis severity on the occurrence of comorbidities, and included 85 women with psoriasis. 65,88% or 56 subjects had comorbidity, ie almost 2/3 of patients. In this study, the most common comorbidities were high blood pressure in 50,59% or 43 subjects, followed by obesity in 38,82% or 33 subjects, dyslipidemia in 30,59% or 26, and diabetes mellitus in 17,65% or 15 subjects with psoriasis.

Other studies have shown the occurrence of high blood pressure, obesity, diabetes, dyslipidemia in patients with psoriasis (Sales et Tores 2014, Souza et al., 2019, Miao et al., 2019, Ghafoor et al., 2015, Girisha et Thomas 2017, El Ghareeb et al., 2019). In our study, the incidence of high blood pressure is indeed high, in more than half of the respondents. psoriasis. (Waqar et Sarkar 2009), but also cyclosporine for the treatment of psoriasis, leads to an increase in blood pressure (Robert et al. 2010). Diastolic blood pressure is more common in women with psoriasis (Uczniak et al., 2017). A review of the literature in 14 of 16 studies revealed an increased incidence of high blood pressure in psoriasis patients compared to control groups (Patel et al., 2011). In a study conducted in the United States, women with psoriasis have an increased risk of developing high blood pressure (Qureshi et al., 2009). Elevated blood pressure was the most common comorbidity in our study, in more than half of the respondents. In a study conducted in India, high blood pressure was also the most common comorbidity in patients with psoriasis (Thomas et al., 2009). As early as 1986, an increased incidence of obesity was detected in women with psoriasis (Lindegard 1986). And obesity doubles the risk of psoriasis (Snekvik et al., 2017), since adipose tissue is metabolically active, secretion of proinflammatory cytokines can lead to worsening of psoriasis (Kunz et al., 2019). Younger women, who do not have a genetic predisposition, are less likely to develop psoriasis if they do not have a high BMI (Naito et Imafuku 2016). A large study, with over 100,000 psoriasis patients, showed that psoriasis is a risk factor for developing diabetes (Azfar et al., 2012). In an observation study with a large number of subjects (almost 65,500), the risk of diabetes in patients with psoriasis increased, higher than in the group without psoriasis, and increased with the duration and severity of psoriasis (Brauchli et al., 2008). A review of 19 studies examining the relationship between dyslipidemia and psoriasis, a significant association between dyslipidemia and psoriasis was found in 17 studies (Daudén et al., 2012). In a study in India, an increased incidence of dyslipidemia was found in 200 women with psoriasis (Kumar and Thomas, 2012).

In this study, the influence of psoriasis severity on the occurrence of comorbidity, ie the correlation between psoriasis severity and comorbidity occurrence, was assessed. There was an association, a positive correlation between the severity of psoriasis, ie PASI score and high blood pressure, but there was no statistically significant association between PASI score and obesity, dyslipidemia and diabetes. Other studies have shown the severity of psoriasis on the occurrence of comorbidities. A literature review of 24 studies involving over 300,000 psoriasis patients found an increased incidence of high blood pressure, and patients with severe psoriasis were more likely to develop high blood pressure than those with mild psoriasis (Armstrong et al., 2013). another study confirmed an association between the severity of psoriasis and high blood pressure (Alexandroff et al.,

2009). Research has shown that obesity is more common in people with psoriasis, and that patients with more severe psoriasis are more likely to be obese than patients with milder psoriasis. The risk of obesity is higher by more than 50% in psoriasis patients compared to the general population (Armstrong et al., 2012) In a systematic review of the association between psoriasis and dyslipidemia, studies that assessed the severity of psoriasis, a higher likelihood of dyslipidemia was observed. In patients with severe psoriasis (Ma et al., 2013). In a UK study, the incidence of diabetes in patients with severe psoriasis was 7,1%, mild psoriasis 4,4%, and in the control group 3,3% (Neimann et al., 2006). There is also an association between PASI score and insulin secretion, and a correlation between PASI score and insulin resistance (Boehncke et al., 2007). The influence of gender on the occurrence of diabetes is also interesting. The incidence of diabetes in psoriasis patients is 1,76 times higher than in the control group, and shows gender differences, the prevalence is 1,93 times higher in women with psoriasis, while in the rest of the population there is no such difference (Ghiasi et al., 2011). In addition to psoriasis, the occurrence of these diseases should certainly be taken into account and the influence of genetic and environmental factors, but also age and other diseases. Some comorbidities may affect the occurrence of others, e.g., obesity, affect the risk and frequency of psoriatic arthritis (Li et al., 2012).

Although research has shown that women have milder forms of the disease a lower PASI score, except for the head area (Hägg et al., 2017), psoriasis is a great burden for women, loneliness and stigmatization are more common, and psoriasis worsens in a quarter of women during pregnancy. An increased risk of preeclampsia, diabetes, high blood pressure and emergency cesarean section has been reported. Therapeutic options are limited in women of reproductive age due to the possible teratogenic effect of drugs (Gottlieb et al., 2019). In addition to the high frequency of comorbidities in almost 2/3 of the subjects (65,88%), high blood pressure in half of the subjects (50,59%), and the fact that 2 comorbidities were present in one fifth of the subjects (20%), 3 comorbidity present in more than a fifth of respondents (22,35%). All of the above should be taken into account in women with psoriasis, in order to receive adequate timely treatment of psoriasis and associated diseases.

Conclussion

Given the frequency of comorbidities, and even the occurrence of more of them in women with psoriasis, their detection and treatment is essential for the comprehensive treatment of psoriasis patients. In addition to the severity of the disease, genetic predispositions, other diseases, age, stress, and lifestyle and habits should be considered when assessing the frequency of screening for associated diseases.

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Skin prick test, total and serum-specific immunoglobulin E in the diagnosis of bronchial asthma

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Abstract

The aim of this study was to investigate the level of total and serum-specific immunoglobulin E (IgE) in 35 children and 35 adults with bronchial asthma over skin prick test. Total IgE measured by the nephelometric method. Serum-specific IgE was measured by enzyme-linked immunosorbent assay for respondents with a positive skin prick test.94.28% of children and 60.0% of adults had elevated tIgE levels. In adults, the skin prick test was more positive compared to sIgE for weed pollen and dermatophagoides pteronyssinus. In children, the skin prick test was more positive compared to sIgE only for weed pollen.This results suggested the skin prick test in kids could be replaced by the sIgE test.

Key words: total IgE, skin prick test, serum-specific IgE, bronchial asthma, enzyme-linked immunosorbent assay.

Introduction

The problem with asthma, both in adults and in children, is not of a recent date, and it is becoming a growing health problem worldwide. It is estimated that there are about 300 million asthmatics globally (1). About 20 million Americans have asthma (2). From 1982 to 1992, there was a worldwide recorded increase in asthma morbidity, by 42% (1- 3). In Bosnia and Herzegovina, data on asthma prevalence, incidence, and mortality are unavailable.

Most patients with this disorder have bronchospasm attacks that are provoked by various allergens, chemical, physical and other stimuli, which is associated with bronchial irritability (4). Allergic bronchial asthma has taken an important place recently. For this type of asthma, an important diagnostic approach is the identification of allergens using skin prick test and serum-specific immunoglobulin E (sIgE) antibody testing (5).

Asthma is a chronic inflammatory disease and today, it is apparent that inflammatory changes are found in the bronchial mucosa of all asthmatics. In patients with episodic asthmas, inflammatory changes are present even at times when there are no symptoms (3,6). Inflammatory elements mainly consist of macrophages, fat cells, dendritic cells, eosinophils, B lymphocytes that are key in the IgE synthesis (reactive antibodies), and T lymphocytes which stimulate eosinophilic inflammation (3, 7). IgE is the least represented antibody class in the serum, present in very low concentrations. With the discovery of this antibody, the era of research in allergology and the field of infectious and parasitic diseases has begun (8). In people with pronounced atopy, antigens cause the production of IgE antibodies that bind to mast cells

in the bronchial tree and basophilic leukocytes in the bloodstream (9). Serum-specific IgE antibody is produced for several weeks after exposure to the allergen and is released into the bloodstream where it can bind to receptors on inflammatory cells, such as mast cells.

The aim of this paper was to examine the levels of total serum IgE (tIgE) and sIgE compared to the results of the skin prick test in randomly selected populations of children and adults diagnosed with bronchial asthma, in order to determine if it is really justified in routine diagnostics for any suspicion of asthma to seek tIgE and then sIgE testing.

Methods

The study included 70 respondents, 35 children ages 0-14 diagnosed with bronchial asthma by a pediatrician - pulmonologist at the Clinic for Children's Disease of the University Clinical Center (UKC) Tuzla (outpatients and inpatients) and 35 adults (older than 14 years) also diagnosed with bronchial asthma by a pulmonologist at the Clinic for Pulmonary Diseases of UKC Tuzla (outpatients and inpatients). The study sample of 35 children and 35 adults was randomly selected after an established diagnosis.

For patients diagnosed with bronchial asthma total IgE levels were quantitatively measured by Siemens Dade Behring BN II Nephelometer (Siemens Healthcare Diagnostics Ltd., Erlangen, Germany) and a skin prick test was performed. Serums of patients were further evaluated for sIgE production by a quantitative, automated enzyme-linked immunosorbent assay (ELISA) method on Hytec 288 (Hycor Biomedical Inc., United States), for all allergens that were determined positive by the skin prick test. A total of 18 allergens were tested by the skin prick test including: grass pollen, weed pollen, tree pollen, wheat, dandelion, hazel, cypress, ambrosia, Candida albicans, Penicillum notatum, animal epithelium, feather, fungus, tobacco, plantain, house dust, Dermatophagoides pteronyssinus (D. pteronyssinus), Dermatophagoides farine, plus positive and negative controls. Respondents that had elevated tIgE levels had a stool sample examined for intestinal parasites by the Kato technique.

This study included subjects diagnosed with bronchial asthma, while subjects who had bronchial asthma diagnosed and stool positive for intestinal parasites, as well as patients with diagnosed carcinoma and/or damaged skin were excluded from the study.

Statistical analysis

Chi-square test was used in evaluation of the categorical variables. P values of < 0.05 were considered statistically significant.

Results

Out of a total of 70 respondents with diagnosed bronchial asthma, included in this study, 29 (41.43%) were male and 41 (58.57%) female (Table 1). Respondents were divided by age into two groups: children, 0-14 years old; and adults, between 14-65 years old. Detailed gender representation of two groups is shown, and it is found to be statistically significant ($p<0.05$).

Table 1. Gender ratio of respondents

Gender	Children (%)	Adults (%)	Total (%)
Male	20 (57.14)	9 (25.71)	29 (41.43)
Female	15 (42.86)	26 (74.29)	41 (58.57)
Total	**35**	**35**	**70**

Skin prick test and total IgE antibody testing were performed for all 70 patients. 94.28% (33/35) of children and 60.0% (21/35) of adults had elevated total IgE levels. Stool examination for intestinal parasites was negative for all patients who had elevated total IgE levels. Relationship between test results of skin prick test and total IgE for children (Table 2), adults (Table 3) and overall, for both groups together (Table 4) are shown. No statistically significant difference has been observed between groups. Statistically significant difference was recorded between males and females in the adult group that tested positive for both IgE and skin prick test, and in children and adults groups together, for patients who tested negative for total IgE and positive on skin prick test.

Table 2. Total serum IgE antibody test results in comparison to skin prick test in children

Children	Male	Female	Total	%
tIgE positive, prick negative	2	0	2	5.71
tIgE positive prick positive	17	14	31	88.58
tIgE negative, prick positive	0	2	2	5.71
tIgE negative, prick negative	0	0	0	0.0
Total	**19**	**16**	**35**	**100**

** tIgE – total immunoglobulin E.*

Table 3. Total serum IgE antibody test results in comparison to skin prick test in adults

Adults	Male	Female	Total	%
tIgE positive, prick negative	2	2	4	11.43
tIgE positive, prick positive	5	12	17	48.57
tIgE negative, prick positive	1	9	10	28.57
tIgE negative, prick negative	1	3	4	11.43
Total	**9**	**26**	**35**	**100**

** tIgE – total immunoglobulin E.*

Table 4. Overall total serum IgE antibody test results in relation to skin prick test in children and adults

Children and adults	Male	Female	Total	%
tIgE positive, prick negative	4	2	6	8.57
tIgE positive prick positive	22	26	48	68.58
tIgE negative, prick positive	1	11	12	17.14
tIgE negative, prick negative	1	3	4	5.71
Total	**28**	**42**	**70**	**100**

**tIgE – total immunoglobulin E.*

Only for allergens that tested positive by skin prick test, sIgE was performed. Comparisons of test results obtained by total IgE and serum-specific IgE in children (Table 5), adults (Table 6) and children and adults together (Table 7) are shown. No statistically significant difference between male and female was observed, nor between positive tIgE and sIgE test results for any of the groups (regardless of gender).

Table 5. Total serum IgE antibody test results in comparison to serum-specific IgE in children

Children	Male	Female	Total	%
tIgE positive, sIgE negative	1	0	1	2.86
tIgE positive, sIgE positive	18	14	32	91.42
tIgE negative, sIgE positive	0	1	1	2.86
tIgE negative, sIgE negative	1	0	1	2.86
Total	**20**	**15**	**35**	**100**

**tIgE – total immunoglobulin E; sIgE - serum-specific immunoglobulin E.*

Table 6. Total serum IgE antibody test results in comparison to serum-specific IgE in adults

Adults	Male	Female	Total	%
tIgE positive, sIgE negative	3	2	5	14.29
tIgE positive, sIgE positive	4	10	14	40.0
tIgE negative, sIgE positive	1	6	7	20.0
tIgE negative, sIgE negative	2	7	9	25.71
Total	**10**	**25**	**35**	**100**

** tIgE – total immunoglobulin E; sIgE - serum-specific immunoglobulin E*

Comparison of positive results of skin prick test and sIgE (listed by allergen) in children (Table 8) and adults (Table 9), as well as the overall correlation for both groups together (Table 10) is shown. In general, there was less difference between skin prick test results and sIgE testing in children than adults, which was statistically significant. In children's group, there was no difference between positive skin prick test and sIgE for house dust, tree pollen and D. pteronyssinus (only negligible 3.33%), while 80% difference was recorded for weed pollen. In adults' group, the greatest percent difference (≥ 50%) was observed for following allergens: weed pollen (54.55%), D. pteronyssinus (56.25%), the animal epithelium (50%), feather (100%), fungus (75%) and tobacco (75%). The most common allergen in children was D. pteronyssinus (Table 8) and in adults house dust (Table 9).

Table 7. Total serum IgE antibody test results in comparison to serum-specific IgE in children and adults

Children and adults	Male	Female	Total	%
tIgE positive, sIgE negative	4	2	6	8.57
tIgE positive, sIgE positive	22	24	46	65.72
tIgE negative, sIgE positive	1	7	8	11.42
tIgE negative, sIgE negative	3	7	10	14.29
Total	**30**	**40**	**70**	**100**

**tIgE – total immunoglobulin E; sIgE - serum-specific immunoglobulin E.*

Table 8. Positive skin prick test in comparison to positive serum-specific IgE antibody testing in children

Children (n=35)			
Allergen	**Prick+ - N(%)**	**Prick+/sIgE+ - N (%)**	**% Difference**
House dust	15 (42.86)	15 (42.86)	0.0
Weed pollen	5 (14.29)	1 (2.86)	80.0
Grass pollen	14 (40.0)	14 (40.0)	0.0
D. pteronyssinus	30 (85.71)	29 (82.86)	3.33

**sIgE – serum-specific immunoglobulin E; D. pt. - Dermatophagoidespteronyssinus.*

Table 9. Positive skin prick test in comparison to positive serum-specific IgE antibody testing in adults

ADULTS (n=35)			
Allergen	**Prick+ - N(%)**	**Prick+/sIgE+ - N (%)**	**% Difference**
House dust	17 (48.57)	11 (31.43)	35.29
Ambrosia	12 (34.28)	7 (20.0)	41.67
Weed pollen	11 (31.43)	5 (14.28)	54.55
Tree pollen	8 (22.86)	6 (17.14)	25.0
Grass pollen	10 (28.57)	6 (17.14)	40.0
D. pteronyssinus	16 (45.71)	7 (20.0)	56.25
Animal epithelium	6 (17.14)	3 (8.57)	50.0
Feather	5 (14.28)	0 (0.0)	100.0
Fungus	4 (11.43)	1 (2.86)	75.0
Tobaco	4 (11.43)	1 (2.86)	75.0

**sIgE – serum-specific immunoglobulin E; D. pt. - Dermatophagoidespteronyssinus.*

Table 10. Positive skin prick test in comparison to positive serum-specific IgE antibody testing in children and adults

CHILDREN AND ADULTS (n=70)			
Allergen	**Prick+ - N(%)**	**Prick+/sIgE+ - N (%)**	**% Difference**
House dust	32 (45.71)	26 (37.14)	18.75
Ambrosia	12 (17.14)	7 (10.0)	41.67
Weed pollen	16 (22.86)	6 (8.57)	62.50
Tree pollen	8 (11.43)	6 (8.57)	25.0
Grass pollen	24 (34.28)	20 (28.57)	16.67
D. pteronyssinus	46 (65.71)	36 (51.43)	21.74
Animal epithelium	6 (8.57)	3 (4.28)	50.0
Feather	5 (7.14)	0 (0.0)	100.0
Fungus	4 (5.71)	1 (1.43)	75.0
Tobaco	4 (5,71)	1 (1.43)	75.0

**sIgE – serum-specific immunoglobulin E; D. pt. - Dermatophagoidespteronyssinus.*

Discussion

Asthma is one of the oldest known diseases. This is the illness of the whole world and it can safely be said to be a disease of the past, the present, and the future (10). It is spread to all parts of the world with a constant tendency of growth in recent decades. In the United Kingdom, bronchial asthma affects approximately 3% and in the United States about 5% of the total population. Lower rates of this illness have been reported in the countries of central and eastern Europe compared to the developed countries of the West. During childhood, boys are more likely to suffer from asthma than girls (11).

Our data showed, in a randomly selected group of children 57.14% (20/35) of boys diagnosed with bronchial asthma and 42.857% (15/35) of girls. Similar results (greater percentage od boys) have been reported by Aberle et al in their epidemiological study of asthma (12). In aforementioned study, there were considerably more boys among the respondents (63.7%) than girls (36.3%). However, in adulthood, women are more likely to be affected than men, as suggested by our results. In our study, out of a total of 35 randomly selected respondents, 9 (25.71%) were men and 26 (74.29%) were women. Similar results were also found by other authors (13). The gender difference in the distribution of asthma in children and adults, observed in our study, was statistically significant.

There are large differences in the prevalence of asthma in rich, moderately rich and poor people in Australia, but it cannot be reliably estimated whether this difference arises as a result of responses to different allergens or other environmental factors, due to more frequent parasitic infections in poorer patients or influences of socioeconomic status in a given country for acquiring the adequate medical care.(14)

Immunoglobulin E is one of the 5 classes of immunoglobulins, suggested to play a major role in asthma immunopathogenesis (15). Normally, in healthy individuals, there is a small amount of IgE, and in a large number of cases, the elevated IgE level indicates anthropic status (16). During infestation with parasites, IgE stimulates the formation of an antibody-dependent, cellular mediated cytotoxic reaction against helminths and parasites. IgE antibodies bind to parasites and direct eosinophilic response against parasites. At a moment when IgE binds to parasites, eosinophils bind to IgE and release toxic products against these pathogens, since helminths and parasites are too large to be phagocytosed. These toxic products can kill, damage or dislodge parasites to protect the host (17, 18). In our research, one of the tasks was to examine the stool for intestinal parasites for patients with elevated IgE levels to exclude parasitosis. However, we did not find any positive results.

In the treatment of allergic diseases and allergic bronchial asthma, of great importance is to avoid the allergen to which the patient is susceptible. Therefore, it is very important to identify the allergen(s). So far, the skin test is considered the most sensitive and most useful method for allergen detection. In this paper, we used a skin prick test. The advantage of this over other skin tests is that it is simpler to perform compared to the scarring and intradermal route, it is less painful and at the same time there is a negligible risk of undesirable reactions. After the completed skin prick test, we performed a serum-specific IgE antibody test by ELISA method for allergens the patients tested positive by skin prick test. Serum-specific IgE testing is a method for detecting and measuring antibodies, which exploits the reaction of enzyme-substrate, whereby the enzyme serves as a marker. Enzymes most commonly bind to antibodies that are specific for some allergens. The amount of enzyme in the antigen-antibody complex is determined indirectly by measuring the amount of degradation product of the appropriate substrate introduced in the final step of the assay procedure. Enzymes which substrates give colored degradation products and enzymes which amount can be easily measured by colorimetry are being used. The most commonly used enzyme is alkaline phosphatase. Degradation of alkaline phosphates substrate, p-nitrophenyl phosphate, gives p-nitrophenol that has an intensive yellow color (19). The advantage of this approach compared to the skin prick tests is that the patient's blood is drawn, the patients go home and return at the scheduled time to get the results. There is no fear of anaphylactic reactions, while the exact allergen concentration in serum is determined. Also, it is not necessary to stop antiallergy therapy before testing.

The most common allergens, which lead to the emergence of allergic sensitization and which, when re-exposing, cause the formation of characteristic symptoms of asthma, can be divided into two large groups: the indoor and outdoor allergens. The indoor allergens are house dust, animal epithelium, dust mites, fungus, insects, cockroaches, and mice urine, and in the outside air there are: various types of pollen, molds and bee/wasp products. Asthma is commonly caused by the following respiratory allergens: house dust, pollen, molds, dermatofagoideus, animal epithelium, feather, insects and industrial chemicals. In our study, positive allergens were: house dust, D. pteronyssinus, Dermatophagoides farine, animal epithelium, trees pollen, weed pollen, grass pollen, ambrosia, feather, fungus and tobacco. In adult subjects, the skin prick test had more positive results compared to serum-specific IgE for house dust by 35.29%, ambrosia by 41.67%, weed pollen by 54.55%, tree pollen by 25%, grass pollen by 40%, Dermatophagoides pteronyssinus by 56.25%, animal epithelium by 50%, feather by 100%, fungus by 75% and tobacco by 75%.

In children population, the skin prick test had more positive results for weed pollen by 80% and D. pteronyssinus by 3.33%, while the results for house dust and grass pollen were concurrent. A similar survey with adult respondents was conducted by Chinoy B et al in 2005 and by Alimuddin et al in 2018 (20, 21). Additionally, our results showed the increased value of total IgE in children with bronchial asthma, present in 94.28% of cases, while 60.0% of adults had increased total serum IgE levels.

Conslusion

Based on the results obtained in our study, it could be suggested that children could replace the skin prick test with specific IgE because the difference between the specific IgE and skin prick test was negligible while in adults there were significantly more positive results on the skin prick test than the specific IgE. The same situation is with the total IgE.

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Frequency of radical syndrome concerning age, sex, and type of occupation

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Abstract

Introduction: The First Instance Medical Commission of Sarajevo Canton (FIMCSC) is an expert body that assesses the health condition of workers/insured persons in the event of temporary incapacity for work for more than 42 days.

Material and methods: Meta-analysis of data for each case (*Individual participant data*) recorded by FIMCSC in the period January 2015- July 2020. A compilation of recorded data, taken from specialist findings, on a sample of 1701 patients, diagnosed with cervical or lumbar radiculopathy. The meta-analysis of the data of each recorded case in the indicated period was intended to present an analysis of the impact of the workplace, gender, and age on the incidence of radicular syndrome. At the same time, we wanted to show the cause-and-effect relationship between diagnosis and profession, as well as the average duration of temporary incapacity for work, due to the current diagnosis.

Results: The largest number of registered patients was within the age group 46 - 55 years (n 621), while the smallest number was registered within the age group 20 - 35 years (n 278). A significantly higher number of patients who are physical workers (> 1200) was recorded, compared with patients from the administrative sector (> 400). Patients with lumbar radiculopathy had the highest incidence, of which the largest number were male patients within the age groups 36 - 45 and 46 - 55 years, physical workers 345 (81%), administrative workers 80 (19%).

Key words: First Instance Medical Commission of Sarajevo Canton, cervical radiculopathy, lumbar radiculopathy, absence from work.

1. Introduction

The First Instance Medical Commission of Sarajevo Canton (FIMCSC) means an expert body that assesses the health condition of workers/insured persons in the event of temporary incapacity for work /absence from work/ for more than 42 days (Federal Rulebook on the Procedure and Criteria for Determining Temporary Disability for the Work of Insured Persons "Official Gazette of the Federation of B&H", No. 34/2017).

The work of FIMCSC is based on the assessment of the current health condition of the patient, analysis and records of the attached specialist findings, as well as the conditions and job descriptions of his workplace.

2. Etiopathogenesis of radiculopathy

Radiculopathy is a disease in which compression and/or irritation of the spinal nerve roots or the nerve itself is present. Compression of the spinal roots is caused by various causes, most often due to disc herniation or thickening of the surrounding ligaments.

Tingling or numbness, until complete loss of sensation as a result of damage to the tactile nerve, are just some of the manifestations of this syndrome (Mesić S et al, 2016). Risk factors for the occurrence of lumbar radiculopathy are repeated activities in longer time intervals, which to a greater extent burden the spinal column. Patients who perform heavy physical work or are professional athletes are more prone to developing radiculopathy than people who spend most of their working time in a sitting position. Other risk factors include age, height, mental stress, and smoking.

2.1 Cervical radiculopathy

Cervical radiculopathy is characterized by neurological dysfunction caused by compression and inflammation of the spinal nerves or nerve roots of the cervical spine (Kyung-Chung Kang et al, 2020). Radiculopathy in the cervical spine is less commonly caused by disc herniation than in the lumbar spine and is usually due to spondylosis, the presence of osteophytes, or a disc-osteophyte complex (Berquist TH, 2013). The pathology of cervical radiculopathy involves compression of the root of the cervical nerve (Rhee JM et al, 2007). Disc degeneration and local ischemia trigger an anti-inflammatory cascade that leads to further sensitization and increased pain in the affected part of the spine (Van Boxem K et al, 2014). Some individuals are suspected of having a genetic predisposition to disc degeneration, although only modest correlations have been found in genome association studies (Sravisht Iyer and Han Jo Kim, 2016).

The incidence and prevalence rate of cervical radiculopathy are unclear, and epidemiological data are limited. Based on studies, it has been confirmed that the incidence of cervical radiculopathy is most common in the fourth and fifth decades of life (Kyung-Chung Kang et al, 2020; Sravisht Iyer and Han Jo Kim, 2016).

2.2 Lumbar radiculopathy

Lumbal radiculopathy is the clinical term used to describe a predictable constellation of symptoms occurring secondary to mechanical and/or inflammatory cycles compromising at least one of the lumbosacral nerve roots. Lumbar radiculopathy is a common health problem among the normal population, which may affect the quality of life, human working capabilities, and may sometimes even cause disability. Degenerative spondyloarthropathies are the primary cause of lumbar radiculopathy (Svetlana Tomić et al, 2009.; Andrew W Tarulli, Elizabeth M Raynor, 2007).

It can also be caused by disc herniation, facet or ligament hypertrophy, spondylolisthesis, or even neoplastic and infectious processes (James A Berry et al, 2019).

The length of the radicular canal increases from the L3 to S1 vertebrae, making the roots of the L5 and S1 spinal nerves more susceptible to compression (Ombregt L, 2013).

Pain is the most commonly reported symptom. However, numbness or weakness along the distribution supplied by the respective nerve root(s) is often appreciated. Radicular pain is typically characterized by patients as “electrical shocks” or “shooting pains” that radiate from the buttock to the foot (Christopher E et al, 2020).

2.3 Occupational radiculopathy

It is not disputed that cervicobrachial or lumbosacral radicular syndromes are more common in workers of certain occupations. However, the frequency, severity of radicular damage, and the length of the painful phase are influenced by numerous factors such as age, body weight, other diseases, length of service, how to use rest during the work process, body position in the work process, presence of vibrations on the work surface and the like. . Due to the high frequency of this syndrome, it is necessary to know all the criteria that must be met for these disorders to be associated with the harmful effects of the workplace and recognized as an injury at work. Physical therapy, correction of lifestyle, and work behavior (training to work safely) are important elements in the prevention of long-term temporary incapacity for work. Back pain is very rarely the result of an injury at work, but in some occupations, it is a work-related illness (Poplašen-Orlovac D., 2011).

Radiculopathy is a very common health problem worldwide and a major cause of disability affecting work outcomes and general well-being.

However, the mitigating circumstance is that most patients with radicular syndrome, in general, go through appropriate medical treatment and recover completely, and only in 5% of patients this pain goes into the stage of chronic disease. In the case when it is considered that the treatment and medical rehabilitation have been and that after its completion there is a decrease in working capacity with remaining working capacity or partial or complete loss of working capacity, the doctor is obliged to send the insured for assessment of working capacity.In Germany and other Western industrialized societies, the radicular syndrome is one of the most expensive health problems.

The European Union and its member states face significant challenges. On the one hand, there is a need to increase productivity and prevent involuntary early retirement, while on the other hand, there is a need to ensure a social system that cares about the aging population. This resulted in a resolution defined by the European Parliament in early 2017. In this resolution, the European Parliament expressed concern over the impact of demographic trends on public finances, pensions, and health systems, and warned that the already projected funding costs would have a significant impact on economic policy coordination. Sip National Platforms [Online] 05 24, 2017. [Cited: 09 22, 2020.]

3. Material and methods

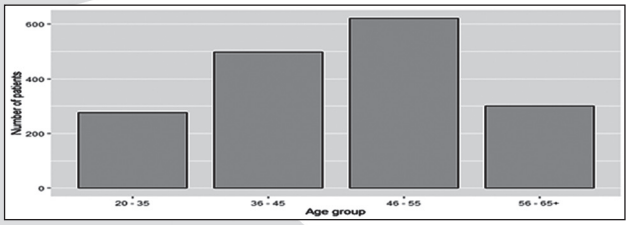
3.1 Test subjects and sample size

The FIMCSC by inspecting the electronic database, performed a meta-analysis of each case that was sent to the same, after 42 days of illness, due to radiculopathy, as a syndrome, within the following diseases, according to the international classification of diseases: M50 - Diseases of the intervertebral discs of the neck: */lat. Morbi discorum intervertebralium cervicalium/*; M51 - Loss of lumbar and other non-vertebral discs with spinal disease /lat. *Prolapsus disci intervertebralis lumb. et discorum intervertebralinum aliorum cum myelo/*. The analysis of the database confirmed that the above diagnoses are among the leading causes of temporary absence from work (sick leave).

The analysis intended to show the cause-and-effect relationship diagnosis-occupation, as well as the factors influencing the occurrence and severity of radiculopathy in the working population (sex, age), in the period January 2015 - July 2020. A meta-analysis was performed on a sample of 1701 patients. Patients were classified according to the diagnoses due to which they were referred to PLJK after 42 days of sick leave, age, sex, and type of occupation (physical and administrative workers). According to age, patients were divided into 4 groups. The first group includes patients aged 20-35; in the second group are patients aged 36-45; in the third group are patients aged 46-55; in the fourth group are patients aged 56-65+ years (Table 1).

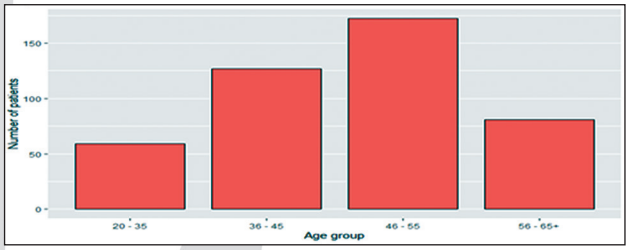
Table 1. Representation of the number of patients concerning age group, sex, and occupation

Parameters		N = 1701	%
Age groups	20-35	278	16
	36-45	500	29
	46-55	621	37
	56-65+	302	18
Gender	M	781	46
	F	920	54
Type of occupation			
Administrative worker	M	149	9
	F	294	17
Physical worker	M	632	37
	F	626	37



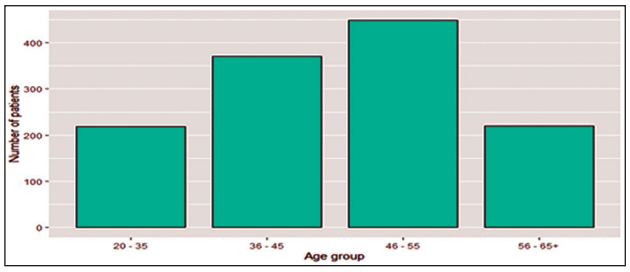
Graph 1. Presentation of the number of registered patients within age groups

The graph shows the largest number of registered patients within the age group 46 - 55 years (n 621), while the smallest number of registered patients within the age group 20 - 35 years (n 278).



Graph 2. Representation of the number of patients with cervical radiculopathy (M50) within age groups

The highest number of patients within the age group 46 - 55 years (> 160) was recorded, while the lowest number of cases was within the age group 20 - 35 years (<75).



Graph 3. Representation of the number of patients with lumbar radiculopathy (M51) within age groups

The largest number of patients within the age group 46 - 55 years (> 400) was recorded, while the age groups 20 - 35 and 56 - 65+ years had almost the same number of registered (> 75).

Graph 4. Comparative presentation of the number of patients by type of work/occupation

A large number of registered patients-physical workers (> 1200), compared to those registered from the administrative sector (> 400).

4. Statistical analysis

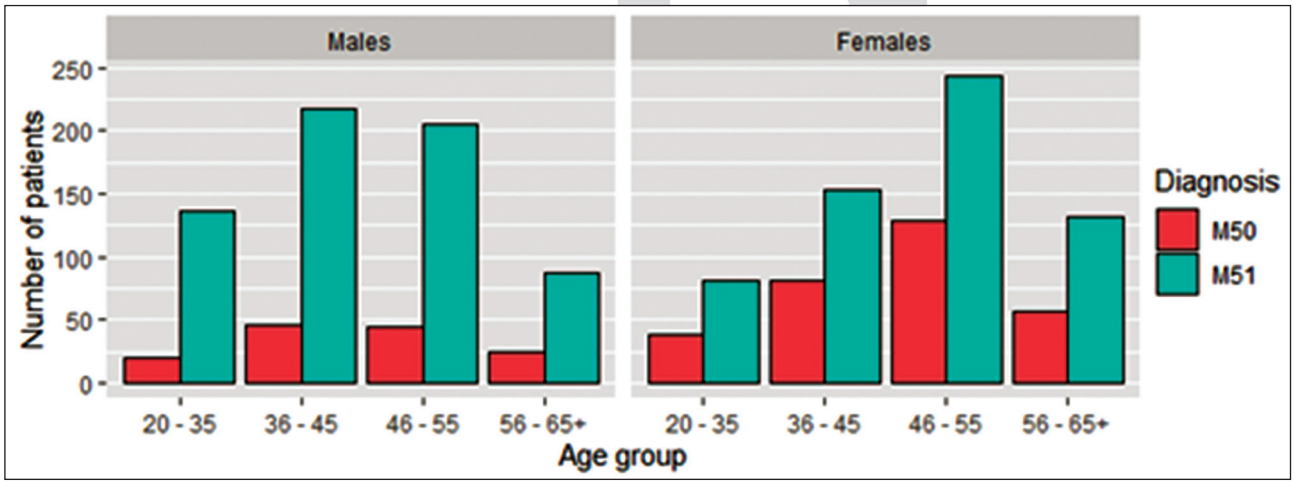
The RStudio application (Open Source Edition, https: //rstudio.com/products/rstudio/), the R programming language in combination with the tidyverse packages (https: //www.tidyverse.org/), was used to analyze the data and create the diagrams.

The meta-analysis of data from each recorded case, in the period January 2015-July 2020 (*Individual participant data*, IPD), was intended to present an analysis of the impact of the workplace, gender, and age on the incidence of radicular syndrome. At the same time, the cause-and-effect relationship diagnosis-profession is presented, as well as the average duration of temporary incapacity for work, due to the current diagnosis. A compilation of accurately recorded data was made, which were extracted by insight into specialist findings, without an impartial interpretation of the attached findings.

4.1 Graphical representation of the analyzed data

The highest number of patients with lumbar radiculopathy (M51) was referred to PLJK KS, of which, the largest number were female patients aged 46 - 55 years (n 250), while the lowest number of cases was aged 20 - 35 (<100). The largest number of male patients was recorded within the age group 36 - 45 years (n 225), a slightly smaller number was recorded in the age group 46 - 55 (n 200), while the lowest number of cases was in the older age group 56 - 65+ years (n 80).

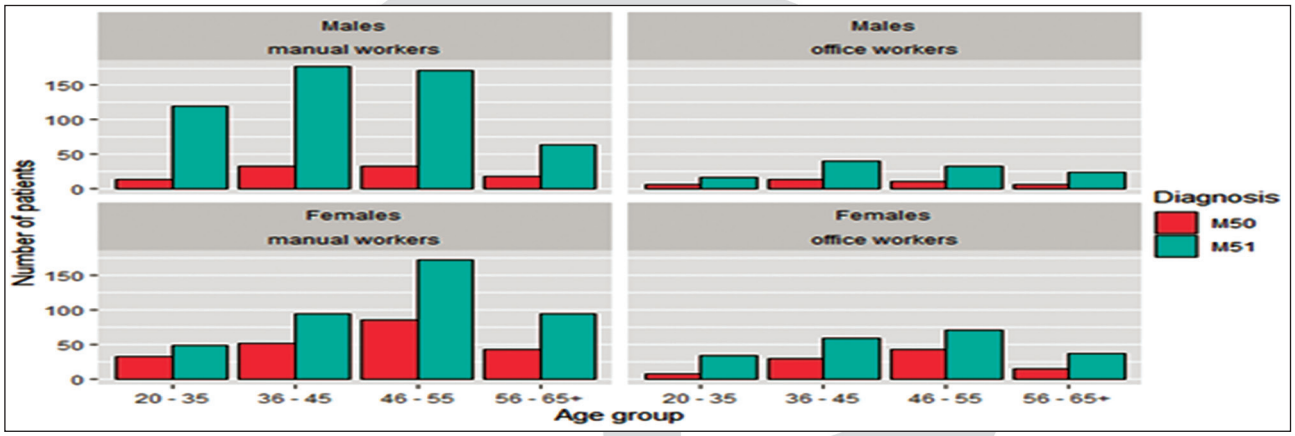
There were a small number of patients with cervical radiculopathy (M50). The largest number of registered patients were aged 46 - 55 years (n 125), and patients aged 36 - 45 years (n 50) and 46 - 55 years (n 48). The lowest number of registered



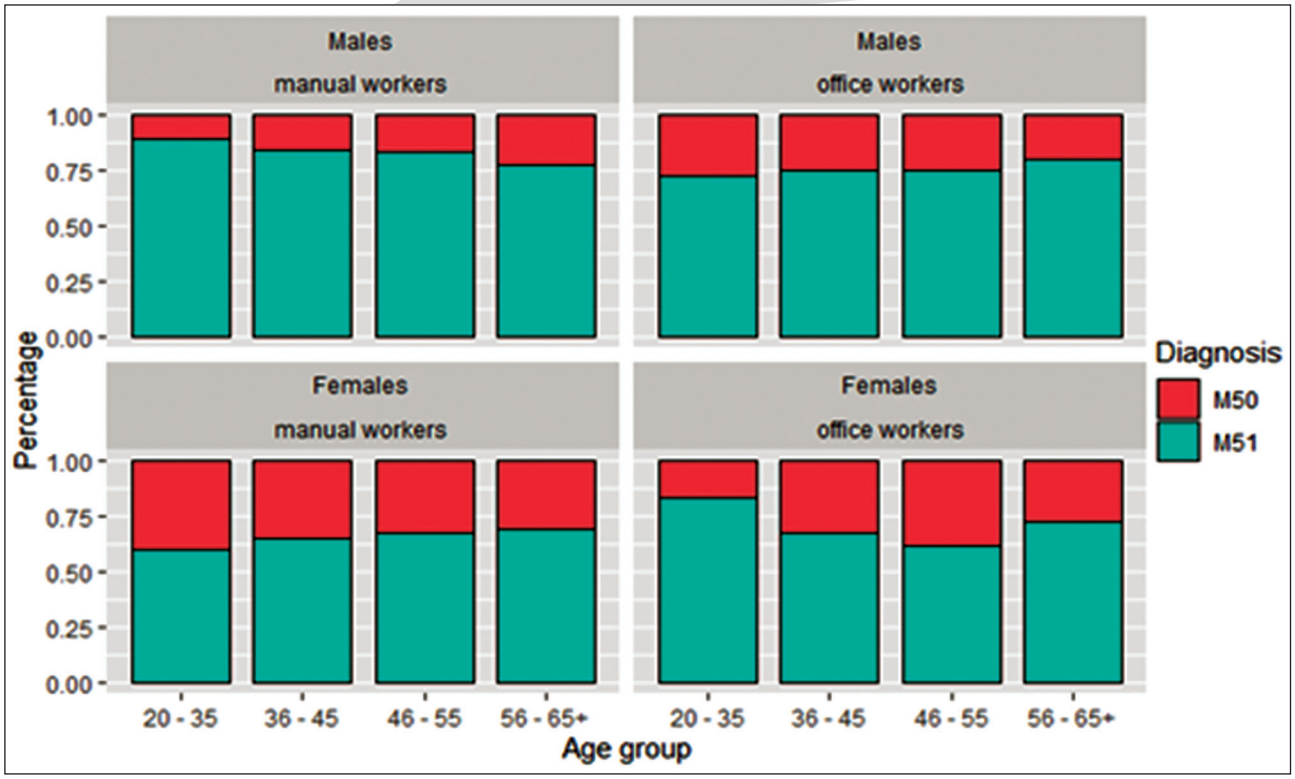
Graph 5. Comparative presentation of the number of patients with cervical and lumbar radiculopathy by sex, age groups, and diagnosis

patients were male patients within the youngest age group 20-35 years (n 25), while a slightly higher number of female patients was recorded in the same age group (n 35).

When the job/occupation parameter is taken into account in the analysis of statistical data, the results show that the highest number of reports is among male patients, physical workers with lumbar radiculopathy, within the age groups 36 - 45 and 46 - 55 years (> 300), while the fewest were recorded within the youngest age group (<25) A smaller number of registered male patients were among administrative workers, 149 in all age groups, of which> 55 with cervical radiculopathy.The highest number of registered patients, physical workers with lumbar radiculopathy, was within the age group of 46-55 years (n 175). The same number was recorded in the age groups 36 - 45 and 56 - 65+ years (n 200). The least recorded were within the youngest age group 20-35 years (n 50).In the age group 46 - 55 years, the largest number of patients, physical workers with cervical radiculopathy (> 75) was recorded, while in the same group in the administrative sector, there



Graph 6. Comparative presentation of the number of patients with cervical and lumbar radiculopathy by age groups, sex, diagnosis, and type of occupation



Graph 7. Comparative percentage of patients with cervical and lumbar radiculopathy by age groups, sex, diagnosis, and type of occupation

were fewer registered patients with cervical radiculopathy (<50). Cervical radiculopathy in patients of physical workers of the younger age group was recorded in a larger number (> 25), compared to patients from the administrative sector, of the same age group (>15).

The highest incidence was reported in patients with lumbar radiculopathy, of which the largest number were male patients in the age groups 36-45 and 46-55, physical workers 345 (81%), administrative workers 80 (19%). female patients are the largest within the age group 46 - 55 years, of which physical workers 175 (68%), administrative workers 80 (32%).

Patients with cervical radiculopathy had a lower incidence, of which the largest number were female patients, within the age group 46-55 years, physical workers 80 (62%), administrative workers 48 (38%).

The lower incidence is made up of male patients, of which the largest number are registered within the age groups 36 - 45 and 46 - 55 years, of which physical workers 60 (70%), administrative workers 25 (30%).

4.2 Overview of the duration of sick leave concerning age groups, diagnoses, gender, and type of occupation

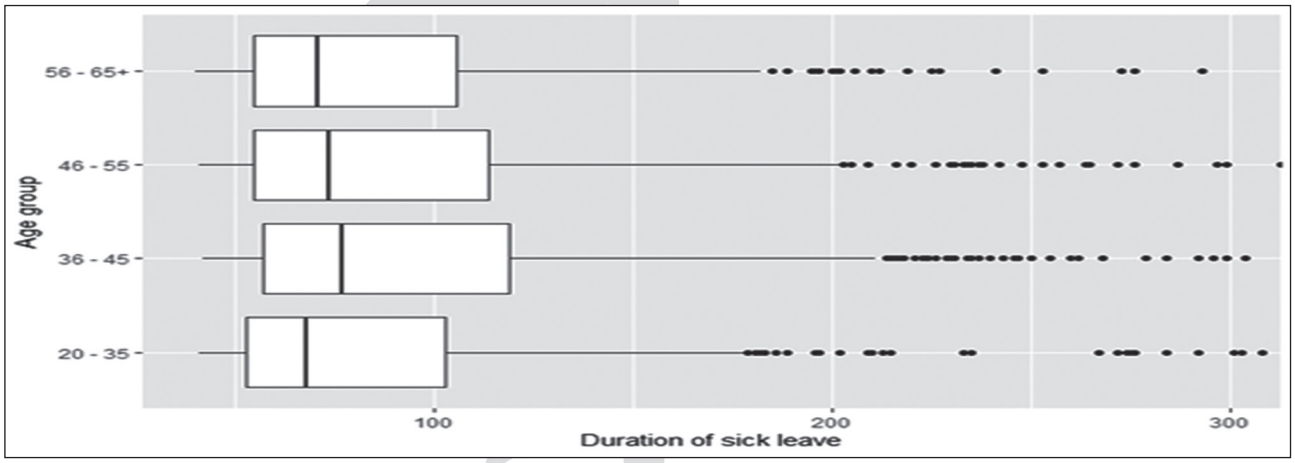
Temporary incapacity for work / sick leave, in the longest range (> 300 days) was recorded within the age groups 36 - 45 and 46 - 55 years.

Temporary incapacity for work/sick leave is recorded as the longest in the diagnosis of lumbar radiculopathy. The sick leave period between 200 and 300 days is significant, while for cervical radiculopathy the ratio is denser between 100 and 200 days.

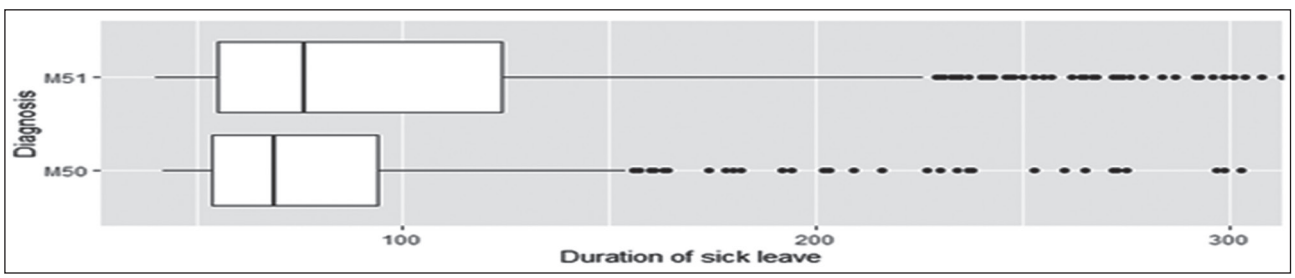
Patients with lumbar radiculopathy within all age groups were temporarily prevented from working within the range of 100 - 200 days, with a point of significance in the age group of 46 - 55 years, which according to statistical analysis were the most recorded.

The prevalence of length of sick leave is in patients with lumbar radiculopathy, of which the predominance is given within 100 days of temporary incapacity for work.

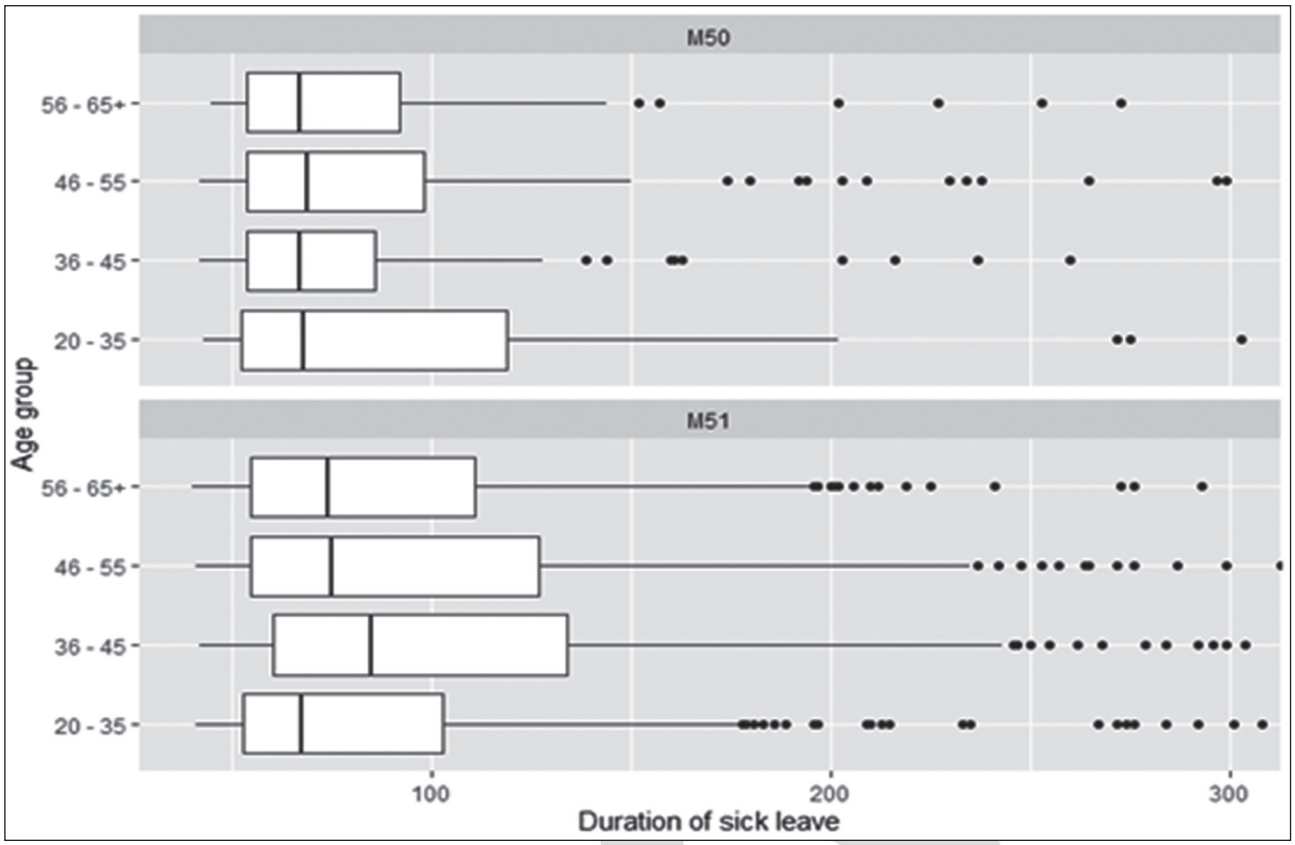
Temporary incapacity for work is recorded longer in female patients, who are engaged in physical work, concerning male patients.



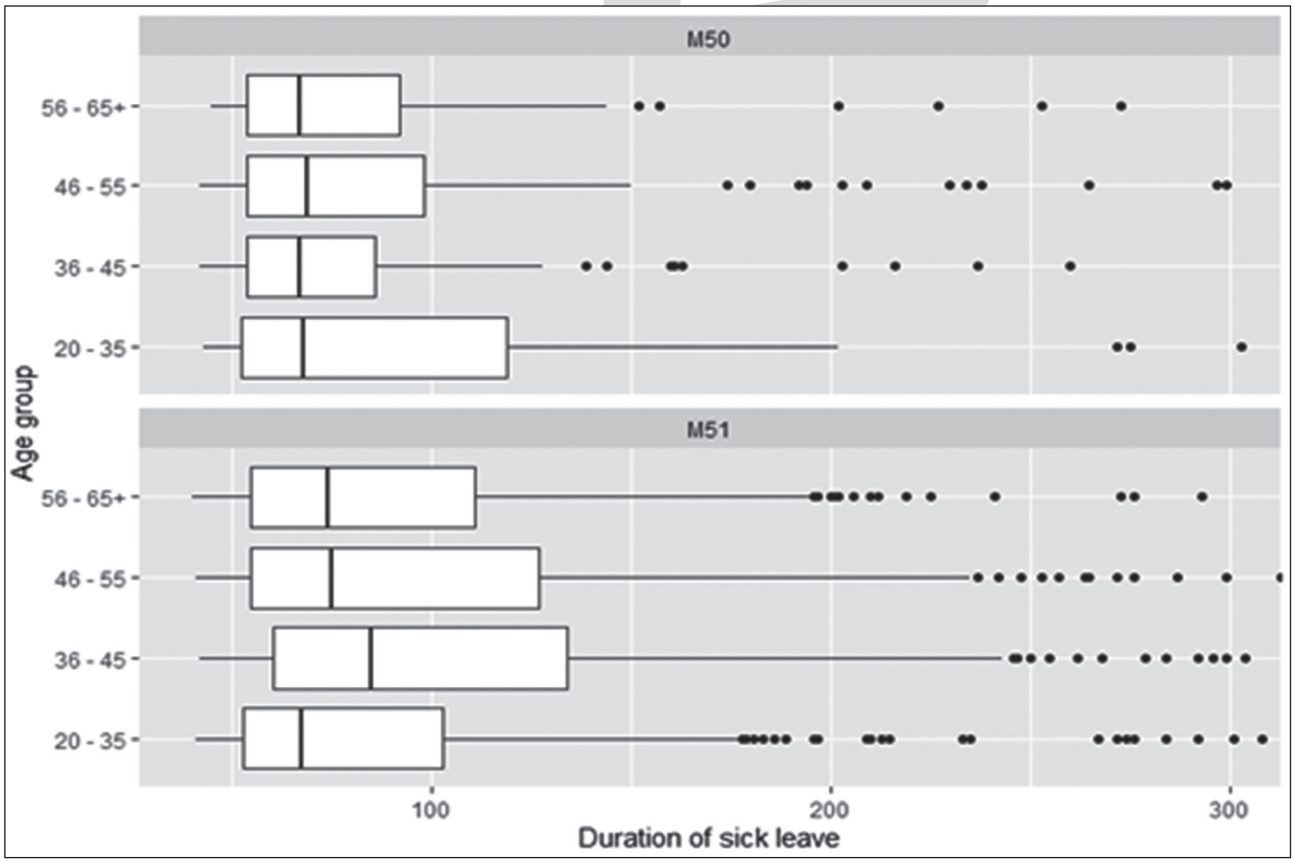
Graph 8. "Box-plot" diagram of the length of sick leave within age groups (scale from 40 to 300 days)



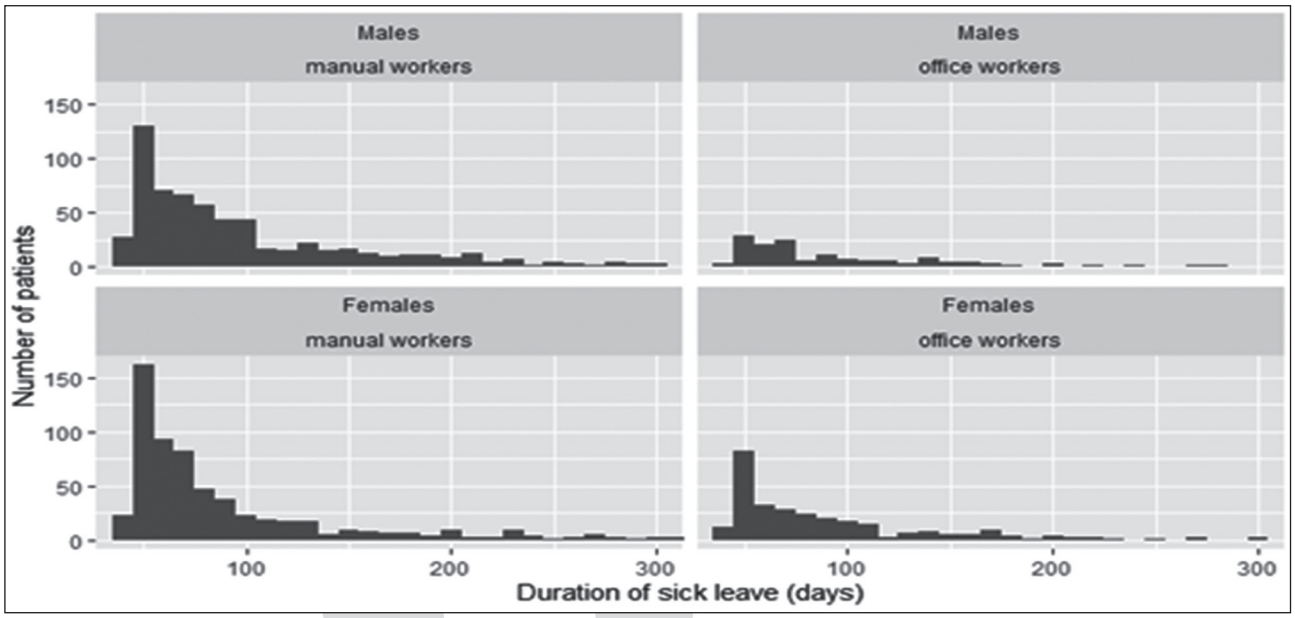
Graph 9. "Box-plot" diagram of sick leave lengths related to diagnoses (scale from 40 to 300 days)



Graph 10. "Box-plot" diagram of the length of sick leave within age groups related to diagnoses (scale from 40 to 300 days)



Graph 10. "Box-plot" diagram of the length of sick leave within age groups related to diagnoses (scale from 40 to 300 days)



Graph 12. Histogram-length of sick leave by sex and type of occupation (column width 10 days, scale from 40 to 300 days)

5. Discussion

About 70% of the world's population experiences back pain at some point in their lives. 30% of adults get sick during the year, of which 5-10% lose their work efficiency. A pilot study conducted in Poland involving 113 randomly selected dental students, up to 32 years of age, found that the relatively high prevalence of cervical spine dysfunction symptoms (chronic pain, stress, immobility) is not the result of their profession alone. the spine is significantly overloaded, but individual predisposition, including the biopsychosocial profile and changing life habits of young people, has a significant impact on their occurrence (Joanna Kuć, Malgorzata Žendzian-Piotrowska, 2020).

Andrew J, Alan A, and others published the results of a study done on members of the U.S. military who were diagnosed with cervical radiculopathy, in the period 2000-2009. About 24,742 people were diagnosed with cervical radiculopathy, among the population at risk of 13,813,333, with an incidence of 1.79 per 1,000 people within one year.

This study is the first to attempt to define the incidence of cervical radiculopathy and characterize risk factors for its development within the U.S. population. The results of the study indicate that the main risk factor for the disease is age (> 40 years) and that women are more likely to get sick (Andrew J Schoenfeld et al., 2012).

Lumbar radiculopathy is the leading cause of disability in the developed world and requires billions of dollars in health care costs annually. Although epidemiological studies vary, the incidence of lower back pain is estimated to be anywhere between 5% and more than 30% with a lifetime prevalence of 60% to 90% (Christopher E. Alexander, Matthew Varacallo, 2020).

The FIMCSC, in the period January 2015 - July 2020, on the processed sample of 1701 patients, the largest number of reports were recorded within the age group 46 - 55 years, 621 registered patients. Of these, the largest number of patients with lumbar radiculopathy, with the analysis found that the largest number of patients were female, aged 46-55 years (n 250), while the largest number of male patients occurred in the lower age group 36 - 45 years (n 225). There were 345 physical workers with lumbar radiculopathy (81%), while there were 80 administrative workers (19%). Patients with cervical radiculopathy had a lower incidence, of which the largest number were female patients, within the age group 46-55 years, physical workers 80 (62%), administrative workers 48 (38%). Temporary incapacity for work in the longest range (> 300 days) was recorded within the age groups 36 - 45 and 46 - 55 years, in both sexes. Patients with lumbar radiculopathy within all age groups were temporarily prevented from working

within the range of 100 - 200 days, with a point of significance in the age group of 46 - 55 years, which according to statistical analysis were the most recorded.

Temporary incapacity for work / sick leave is a major burden on each country's health system. The length of treatment of radicular syndrome will depend on many factors, the greatest importance of which should be given to the job description. Jobs that involve more physical exertion require a longer recovery. If the patient fails to establish the ability to return to work (within 1 year of treatment), FIMCSC refers the patient to the assessment of working ability (Article 10 of the Federal Ordinance on temporary incapacity for work), based on which the employer is obliged to provide the insured workplace following the assessment given by the expert body that assessed the patient/worker.

6. Conclusion

The FIMCSC, in the period January 2015 - July 2020, on a processed sample of 1701 patients, the largest number of cases was recorded within the age group 46 - 55 years. Lumbar radiculopathy, concerning age, most often occurs in women in the period of 46-55 years of age, while in men it occurs almost equally often in the period of 36-45 and 46-55 years of age. When the parameter work/occupation is taken into account in the processing of statistical data, the results show that the highest number of reports among male patients, physical workers, is in the age groups 36-45 and 46-55 years.

There were fewer registered patients with cervical radiculopathy, of which a larger number were women aged 46-55, who performed physical work. In the administrative sector, a larger number of female workers suffer from cervical radiculopathy than men.

Temporary incapacity for work / sick leave is recorded the longest in patients with lumbar radiculopathy, aged 46 - 55 years, of which the predominance is given to a period within 100 days of temporary incapacity for work.

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Biochemical parameters in patients affected by psoriasis

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Abstract

Background: Psoriasis is a chronic disease, and research among those affected by it have shown a higher occurence of other diseases, such as obesity, metabolic syndrome, cardiovascular diseases, diabetes, hyperlipidemia, Crohn disease, and changes in the values of C-reactive protein (CRP) as well as fibrinogens, homcisteins, folic acid. Aim of the research: To determine the values of biochemical parameters, CRP and fibrinogens in patients affected by psoriasis with comorbidity (metabolic syndrome, obesity, diabetes, high blood pressure, dyslipidemia) and without comorbidity.

Respodents and methods: Prospective research was contudcted which included 120 examinees affected by psoriasis split into two groups, with and without comorbidity.

Results: Values of fibrinogen in group with comorbidity were statistically higher than in the group without comorbidity ($t=5,17$; $p<0,0001$). Values of CRP in group with comorbidity were statistically higher compared to the group without comorbidity ($t=2,70$; $p<0,01$).

Conclusion: CRP and fibriongen tend to be elevated in patients affected by psoriasis with comorbidity, which supports psoriasis being a sistematic inflammatory disease.

Key words: psoriasis, comorbidity, C-reactive protein, fibrinogen.

Introduction

Psoriasis is a chronic disease which manifests through erythematous plaques covered by whiteish squama/scales. It is of unknown etiology, and research has shown that psoriasis patients have a higher frequency of other diseases, such as obesity, metabolic syndrome, cardiovascular diseases, diabetes, hyperlipidemia, Chron's disease, and changes in the values of CRP and fibrinogen, homocistein, folic acid (Augustin et al., 2010, Gisondi et al., 2010). Multiple research has shown increase in values of CRP and fibrinogen in patients affected by psoriasis (Dowlatshahi et al., 2013, Warnecke et al., 2011, Alpsoy et al., 2014, Kustan et al., 2018).

CRP is a protein of the acute inflammation stage, synthesized in liver and elevated in multiple conditions, including psoriasis (Pepys et Hirschfield 2003, Paller et Pertrou 2019). Fibrinogen is a glycoprotein which has numerous roles, such as coagulation, wound healing, vasoconstriction (Gabay et Kushner 1999). Elevation of fibrinogen found in patients affected by psoriasis, is also linked to a higher risk of a heart attack, stroke (Danesh et al., 2005). Elevated levels of CRP and other inflammatory cytokines, patients may also have an increased risk of cardiovascular diseases, and it can also affect the longevity of life (Siegel et al., 2013). All of that changes the image of psoriasis from skin to a more systematic disease, but also the approach to the patients, where it is not necessary to only treat the changes on the skin.

AIM

To establish the values of biochemical parameters, CRP and fibrinogen in patients with psoriasis and comorbidity (metabolic syndrome, obesity, diabetes, elevated blood pressure, dyslipidemia) and without comorbidity.

Respodents and methods

This is a prospective research. Experimental group consisted out of 70 test subjects, affected by psoriasis with comorbidity (metabolic syndrome, obesity, diabetes, elevated blood pressure, dyslipidemia of both genders, aged 18 and older. Average age was 47,14 (SD= ±15,41), 36 men or 51,43% and 34 women or 48,57%. The average duration of psoriasis was 15,52 (SD=±12,54) years.

Control group consisted out of 50 test subjects, affected by psoriasis without comorbidity, both genders, aged 18 and above. The average age was 47,28 (SD =±14,37), out of that 26 men or 52% and 24 women or 48%. The average duration of psoriasis was 15,15 (SD=±12,26).

The most common type of psoriasis was psoriasis vulgaris 80%, then psoriasis guttata 15,71%, psoriasis palmoplantaris 4,29% when it comes to the experimental group, and in control group, the most common was psoriasis vulgaris 76%, psoriasis guttata 16%, psoriasis palmoplantaris 6%, psoriasis pustulosa generalisata 2%.

Researach involved patients with diagnosed cases of psoriasis, medical records from a dermatovenerologist as well as patophysiological records, whom were treated at the clinic for skin disease of University clinical center in Tuzla. Research did not involve patients who besides psoriasis had additional skin diseases, as well as those who suffered from psoriasis for a period of less than a year or have been using systmetic medicine for psoriasis.

Research was approved by the Ethical commitee of the University clinical center in Tuzla. Test subjects were briefed on the purposes of the research, they were asked for written confirmation of their participation, had their medical history taken, dermatological skin analysis conducted as well as visible mucos membranes. After that, they were subjected to the tests. All of the subjects involved in the research were checked for metabolic syndrome, obesity, elevated blood pressure, diabetes and dyslipidemia. They had biochemical search done for proteins of acute inflammation (CRP and fibrinogen). Levels of CRP and fibrinogen were checked using standard biochemical procedures, after taking blood samples from the vein who have not consumed food for the period of at least 8 hours prior.

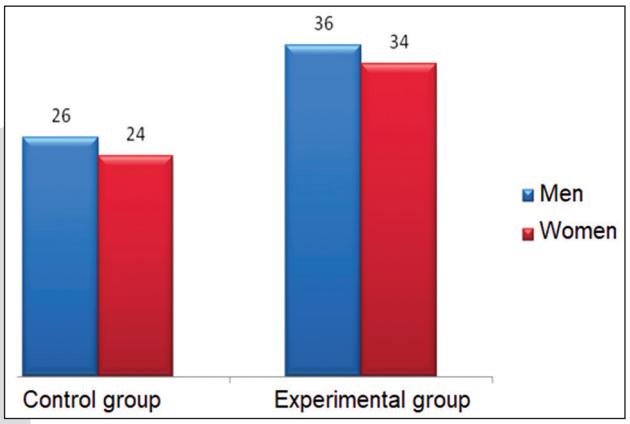
Reference values of CRP 0-3,3 mg/l. Reference values of fibrinogen: 0,3.5 g/l

Statistical methods

For the processing of data and hypothesis tests, statistic package Arcus Quickstat Biomedical Version 1.0 was used. Difference between the groups were estimated using a t-test. As a smallest base value, p<,0,05 was taken.

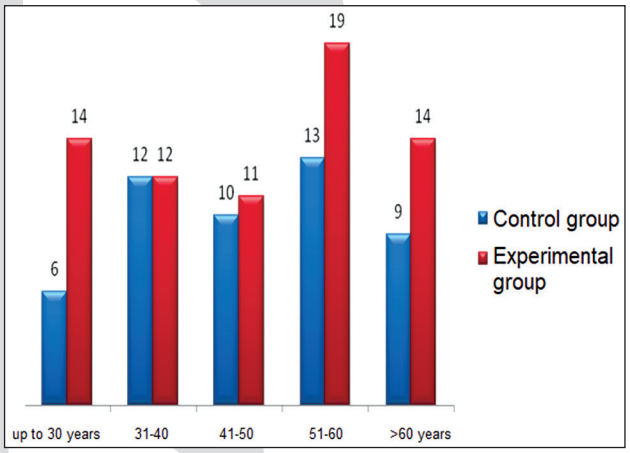
Results

Gender structure of psoriasis patients was balanced in both control and experimental groups (Picture 1).



Picture 1. Gender structure of psoriasis patients

Age structure of psoriasis patients was balanced in both the control and experimental groups. (Picture 2).

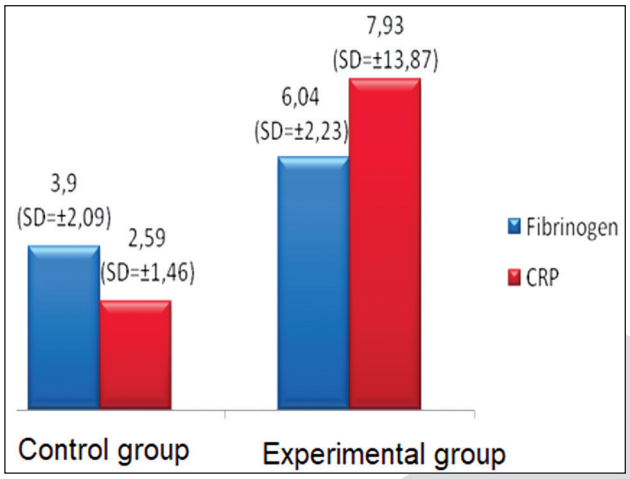


Picture 2. Age structure of psoriasis patients

Average age of the test subjects inside the control group was 47,28 years (SD=±14,37) and in experimental group, that number was 47,14 years (SD=±15,41).

Biochemical parameters in psoriasis patients

Average values of fibrinogen and CRP in the patients suffering from psoriasis are shown in picture 3.



Picture 3. Fibrinogen and CRP values in patients with psoriasis

Values of fibrinogen in the experimental group were statistically much higher compared to the control group (t=5,17; p<0,0001)

Values of CRP in the experimental group were statistically higher compared to the control group (t=2,70; p <0,01).

Discussion

Psoriasis is a chronic inflammatory, uncurable disease, and as such it has a huge impact on all aspects of life of the patient. It has for a very long time been considered as a purely skin disease, and patients were seen as otherwise "healthy" and as such, not a lot of attention was given to it like in the cases of some other chronic diseases. Treatment of the skin aspect is insufficient, considering that it can be followed by significant and serious comorbidity as well as changes in the biochemical parameters.

In this research we have analysed the values of CRP and fibrinogen in the patients suffering from psoriasis with comorbidity (metabolic syndrome, obesity, diabetes, elevated blood pressure, dyslipidemia–experimental group) and without comorbidity (control group). Average value of CRP in patients suffering from psoriasis with comorbidity (experimental group) is 7,93, SD=±١٣,٨٧) and is higher than in the patients without comorbidity (control group) 2,59,SD=±1,46; (t=2,70; p<0,01). Average value of fibrinogen in the patients suffering from psoriasis with comorbidity is 6,04 (SD=±2,23) and it was higher than in the patients without comoribdity 3,9 (SD=±2,09). (t=5,17; p<0,0001). In this research, values of CRP and fibrinogen were elevated in the experimental group, fibrinogen was also elevated in the control group beyond the reference values, while CRP in the control group was inside the reference values.

Other research has also shown elevated values of CRP and fibrinogen in patients suffering from psoriasis with comorbidity, so in the research of Usta et al. (2011), levels of CRP and fibrinogen were moderately elevated in patients suffering from psoriasis compared to the control group (p=0,008 ip=0,011). As well as Lora et al. (2013), who found levels of CRP to be higher in patients suffering from psoriasis than in the control group. Research conducted in Portugal has also found that CRP is in correlation with the severity of psoriasis (Coimbra et al., 2013). Target of the analysis which encompassed 63 studies, shown that levels of fibrinogen and CRP were elevated in psoriasis patients (Bai et al., 2017).

Although, in the available literature, no comparison of values of CRP and fibrinogen in psoriasis patients with and without comorbidity was found, Arias-Santiago et al. (2012) have found elevated values of CRP and fibrinogen in patients suffering from psoriasis when compared to the control group, but also that CRP and fibrinogens were higher in patients suffering from psoriasis with metabolic syndrome, than in the patients without it.16 There was also a possitive correlation of CRP and fibrinogen with abdominal obesity and triglycerides.In the research done by Paschoal et al. (2018) levels of CRP was elevated in patients suffering from psoriasis with metabolic syndrome, and arterial hypertension, and risk of metabolic syndrome was linked with elevated CRP. Measuring and control CRP is important for numerous reasons. Research has shown that lower levels of CRP after treatment confirm that tracking levels of CRP can serve as an important prognostic tool when grading response to the treatment (Isha et al., 2011). Increase in acute inflammation measured by levels of CRP is laso linked to a higher mortality rate and is almost twice as higher compared to the patients who have seen a drop in those levels (Poole et al., 2009).

To conclude, CRP and fibrinogen were elevated in patients with comorbidity and psoriasis, which supports the hypothesis that psoriasis is a systemic inflammatory condition. Control in values of CRP

and fibrinogen can be the first step in prevention, or even treatment, and further research is needed in order to see their applications as biomarkers for the apperance of comoribidity in patients suffering from psoriasis. Besides treating skin changes, and taking into consideration all recent findings about psoriasis, it is important to track, prevent or even treat associated diseases.

Conclusion

Psoriasis is a chronic inflammatory condition, and patients suffering from it may have changed values in the levels of CRP, fibrinogen and comorbidity, which advocates for a systemic disorder. There, controls of CRP and fibrinogen are necessary for psoriasis patients, because it is readily available, cheap, quick and easily conductible, not overly aggresive for the patient and is a first step in discovering or even preventing comorbidity.

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SSRI Antidepressant Side Effects in Depression Patients in the first 6 months of treatment

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Abstract

Introduction: Treatment with antidepressants is associated with the risk of a poor response to treatment and lifelong depression. The aim of this study is to evaluate success and treatment of the most common l prescribed antidepressants Paroxetine, Sertaline and Flusetine in relation to adverse reactions and relapse symptoms of the clinical picture of depression.

Methods and Respondents: The research was designed as a prospective, transient study voluntarily on a voluntary basis and with respect to anonymity, during 2013-2014. The study was included patients treated for depression without psychological symptoms. The research instruments were the Hamilton scale for the evaluation of depression (12) and the Toronto scale of adverse reactions to antidepressants (13). In the overall sample of respondents (n = 349), respondents were continuously treated with one of the 3 SSRI the most frequently prescribed antidepressants (Paroxetin, Sertalin or Flusetin) in the current episode of depression, lasting up to 6 months. The spinal focus group consisted of n = 176 subjects.

The average age of the subjects is 48.55 ± 9.74 years, and the female is 62%.

Results: The average values of Σ depression 20.27 ± 8.396 reveals that respondents are mostly suffering from a serious episode of depression. Success in withdrawal of symptoms and achievement of remission in the first 6 months is achieved with the following frequency: 8% during treatment with Paroxetine (Seroxat); 0% during treatment with Sertraline (Zoloft); and 6% during treatment with Flusetine. The failure to treat depression and the inability to achieve remission of the disease is statistically significantly correlated with the selected antidepressant (Speraman correlation factor = -0.141, P = 0.008). If you treat depression with Sertalin, then it might appear suicidal intentions in 12 % of responedents.

Conclusion: The outcomes of treatment most commonly prescribed by SSRI antidepressants in the first 6 months are very poor. It seems appropriate to control the adherence of SSRI antidepressants and improve pharmacotherapy with psychotherapy.

Key words: treatment of SSRI antidepressants in the first 6 months, Paroxetine, Sertalin, Flusetin, failure of treatment due to the inability to achieve symptoms remission.

Introduction

Depression is an episodic disorder, and in 50% to 80% of people who has the first depressive episode, a new, repeated depressive episode will appear definitely. Depression is a disease accompanied by a reduced mood, which changes the overall thinking, observation, physical condition, behavior and social function of a person (1). The untreated depressive episode lasts between 6 and 13 months on average, and most are treated for two to three months (2.3). The most frequently prescribed SSRI antidepressants are: Paroxetine (Seroxat) 57.3%, Sertalin (Zoloft) 11% and Fluoxetin (Flusetin) 41.15% (4.5). Typical symptoms in the clinical picture are: depressed mood, loss of interest and satisfaction in everyday and early activities, reduced energy and reduced self-esteem. Often, there are outbursts of cry or inability of a person to cry and feel emotions (6). Almost 80% of patients report sleeping problems, most commonly with difficulty sleeping or early morning awakening. In addition to sleeping problems, there is a decrease in appetite in many patients with a consequent loss of body weight (7). Other common symptoms of depression include a reduction in the interest in sexual activity, which may sometimes result by referring person to

spouse therapy, and sometimes it that depression is not recognized or treated beforehand (8).

Antidepressants are a group of drugs that primarily improve depression, stimulate vital dynamisms and act anxiolytic (6). Their effect is based on the knowledge of the functional disadvantage of "monoamine" in depressive disorder. Thus, antidepressants are synthesized that increase the concentration of monoamines at the receptor sites in the brain. They affect the change in the number and sensitivity of monoamine energetic receptors. *Noradrenaline* and *serotonin* are the most important monoamines.

Thus, the increase in serotonin leads to mood enhancement, and noradrenaline affects at motor skills and behavior (9). The role of the third neurotransmitter, *dopamine*, is not insignificant. It is significant at the stage of transition of depression to mania. Having in mind all this knowledge about neurotransmitters, a large number of drugs with selective action on a certain subtype of the receptor have been synthesized. Antidepressants are usually given to patients for 2-3 months. More often in practice we have the situation that after the withdrawal of symptoms of the patient's disease, the same dose is administered for another 3-6 months, as this procedure has been shown to prevent recurrence of the disease (2, 3,11).

The aim of this study is to evaluate the success and treatment most commonly prescribed by antidepressants Paroxetine, Sertaline and Flusetine in relation to adverse reactions and the relapse symptoms of the clinical picture of depression.

Methods and respondents

The research was designed as a prospective, transient study by volunteering on a voluntary basis and with respect to anonymity, during 2013-2014. The study included patients treated with a mild and moderate form of depression without psychological symptoms, and receiving antidepressant medication in pharmacies in Tuzla. The research instruments were Hamilton's scale for assessing depression (12) and the Toronto scale of adverse reactions to antidepressants (13). The study was approved by the Commission for Ethical Issues of the Pharmaceutical Chamber.

The total sample included 349 respondents of 500 involved (response to the survey 69.8%). Including the factor for the respondents was: diagnosed depressive disorder without psychotic symptoms; respondents aged 19-65 years. In the overall sample, respondents who are continuously treated with one of the 3 SSRIs are the most frequently prescribed antidepressants (Paroxetine, Sertalin or Flusetin) in the current episode of depression, for up to 6 months as respondents. The respondent focus group consisted of n = 176 respondents.

Statistical data processing

For the analysis of results, the standard Statistical Package for Social Research (SPSS) version 19.0 was used. Statistical processing of the results was carried out using standard methods of descriptive statistics. X2-test and t-test were used to test the statistical significance of the difference in the selected variables. A non-parametric Sperman test correlation was used for multivariate correlation analysis.

Results

The average age of the subjects is 48.55 ± 9.74 years, the average height is 171.66 ± 8.689cm and the average weight is 77.18 ± 15.824kg. Mean value Σ of depression 20.27 ± 8.396 reveals that respondents mostly suffer from a serious episode of depression.

The highest number of respondents is female 217 out of a total of 349 (62%), and they are 41 to 60 years of age (67%). Depressive disorder is most commonly represented in the most educated, with 59% of those with a university degree and 36% with a completed secondary school (Table 1)

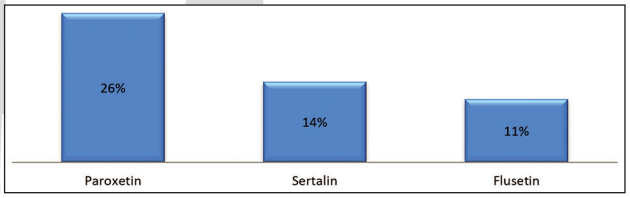

Figure 1. Distribution of respondents according to selected SSRI antidepressants.

Most respondents were treated with antidepressants only 239 (68%) of 349 patients. N = 175 were treated with the most commonly prescribed SSRI antidepressants: Paroxetine 26% (n = 89), Sertaline 14% (n = 50) and Flusetine 11% (n = 36) (Picture 1).

Table 1. Structure of respondents according to individual characteristics and demographic data

Characteristics of respondents	No= 349 Number of respondents n	Frequency %
Gender		
Male	132	38
Female	217	62
Age group (years)		
<30	11	3
31-40	51	15
41-50	116	33
51-60	120	34
>60	51	15
Activities		
Administrative, health care service and others unproductive	427	94
All productive	22	6
Educational level		
Elementary school	2	0.6
Professional education	17	4.4
High school	125	36
Higher education	205	59

In general, failure while treating patients with antidepressants in the first 6 months is unexpectedly high. The most difficult remission of depressive episode symptoms is achieved by treatment of the most frequently used by antidepressant (Figure 1). It may be a problem by neglecting the etiological factors of depression in treatment, inadequately determined diagnose during initial drug choice, inadequate treatment approach, and inadequate evaluation of the effects of treatment in time or drug resistance.

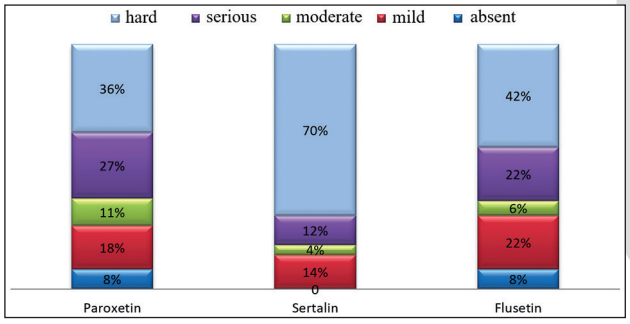

Figure 2. Comparative structure of suicide cases at respondents according to selected SSRI antidepressants

During the treatment by the most commonly prescribed antidepressants in the first 6 months, the success in withdrawing symptoms and achieving remission in general is possible with the following frequency: 8% during treatment with Paroxetine (Seroxat); 0% during treatment with Sertaline (Zoloft); and 6% during treatment with Flusetin (Figure 2).

A severe episode of depression as the most difficult clinical form of the disease and the biggest symptoms that present failure during treatment was found at patients who were treated by: Paroxetine 36%, Sertaline 70% and Flusetine 42%. The rate of severity of a serious episode of depression was distributed in: 37% of Paroxetine treated patients, 14% of patients treated with Sertraline and 22% of patients treated with Flusetine. The unexpected results was treatment by Sertaline (Zoloft) because 70% of the treated patients suffer from a severe episode of depression, 14% serious, 4% moderate, and 12% mild episode (Figure 2). A complete remission treatment with Sertalin was not achieved by any respondent. There is statistically significant difference in the different outcome of the treatment failure in relation to the different choice of the antidepressant ($\chi 2$ test = 49.943, P = 0.000, P <0.001).

The failure of treating depression and the inability to achieve remission of the disease significantly correlates with the selected antidepressant (Speraman correlation factor = -0.141, P = 0.008).

In Figure 3, the comparative structure of suicide is shown according to the most prescribed SSRI antidepressant. The prevalence of perception that life is not worthwhile is almost uniformly frequent and without significant differences compared to the choice of SSRI antidepressant: Sertaline 28% and Fluxetine 28% and Paroxetine 27%. It can be assumed that is the usual occurrence of SSRI treatment by antidepressants in the first months. Similar situation exists in estimating the rate of suicide reports: Sertaline 5% and Fluxetine 4% and Paroxetine 5%.

It is deeply concerned the fact of perception the suicidal intentions during treatment by Sertalin with the rate of prevalence of 12%. The level of suicide is statistically related with the chosen antidepressant (Speraman correlation factor = -0.141, P = 0.008).

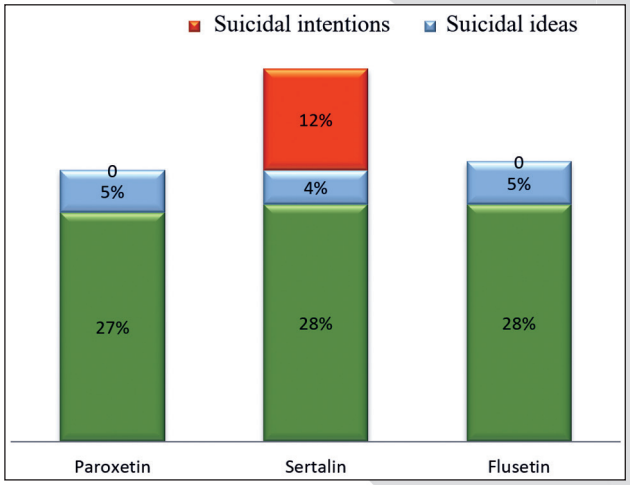

Figure 3. Comparative structure of suicide at respondents according to selected SSRI antidepressant

Discussion

Every treatment with antidepressants was followed by side effects, but the profile of the side effects with the new antidepressants changed significantly. After acute treatment of depressive disorder, the remaining symptoms are common. Patients with residual symptoms of depression have an increased risk of relapse and recidivism (14). Depression usually occurs at people who have had panic attacks or long-term anxiety for some time (1.15).

The improved tolerability of SSRI antidepressants in relation to other antidepressants is attributed to their selectivity and the absence of interaction with other receptors, such as histamine, cholinergic, dopaminergic and noradrenergic (16). However, serotonin receptors contain at least 7 classes that are further subdivided into the subreceptor level. These receptors mediate various non-mood functions including sleep, appetite, and sexual function, as well as symptoms such as pain, nausea, depression, and anxiety (8.17).

Selective serotonin inhibitors stored (SSRIs) are currently the first choice for depression therapy (19). In general, failure of treatment with SSRI antidepressants at our respondents in the first 6 months is unexpectedly high. The most difficult remission of symptoms of depressive episode has been achieved by treatment of the most recommended and used SSRI, Paroxetine and Sertalin. It should be noted that antidepressants have proven their effectiveness in the treatment of acute depressive episodes and the prevention of relapse for a long period of time (20). Research shows that psychotherapy can play an important role in enhancing the effects of antidepressant therapy, and can improve patients' long-term prognosis. Psychotherapy has certain goals related to the recurrence of symptoms of guilt, hopelessness, negativism and low self-esteem. It is known that antidepressants cannot reduce the irritability that is most effectively enhanced by the management of stress. In this way, in the long term, health improves and stimulates cognitive changes. The results were confirmed in the modulation of critical common goals of treatment and facilitating depression remission during joint treatment with psychotherapy and pharmacotherapy in various parts of the cortical-limbic pathway. The use of ancillary psychotherapy in the acute phase of depression treatment seems to give only a modest increase in the rate of expected therapeutic responses. The simultaneous usage of pharmacotherapy and psychotherapy during the maintenance phase inconsistently gives a clear advantage over maintenance of pharmacotherapy (14).

However, whether due to inexperience of the chronicity of depression or because of intolerable adverse effects or inappropriate fear of addiction, treatment with antidepressants is often interrupted after remission or recovery from an acute episode, which often leads to recidivism of the disease. This, however, increases the risk of poor response to

treatment and lifelong depression (21). It may be a problem in neglecting the etiological factors of depression in treatment, inadequately diagnosed during initial drug choice, inadequate treatment approach, and inadequate evaluation of the effects of treatment in time or drug resistance. Social theories emphasize the role of stress, assuming that a series of stress staging predisposes a person for the development of depression. There are surely also the premorbid personality traits that can represent a good basis for the development of this disorder (22). What is confirmed suggests that the choice of a particular SSRI ($\chi 2$ test = 49.943, P = 0.000, P <0.001) is very important for the different outcomes and success for treatment with SSRI antidepressants.

Patients treated with SSRI antidepressants continuously without interruption in the first 3 months experience a lower risk of relapse and recidivism (risk ratio: OR = 0.42, 95% CI, 0.40 to 0.44). Also, patients who have three or more control visits to a psychiatrist or a selected physician in the first 3 months also reduce the risk of relapse / recidivism. Factors associated with a significant increase in relapse / recurrence are comorbidity chronic diseases, anxiety disorder and alcohol consumption (23).

Insomnia, irritability and anxiety occur occasionally in early stages of treatment. Several patients discontinued Flusetine treatment due to adverse reactions and the least treated Sertalin (24). Our results are contradictory. Unexpectedly, there is a poor therapeutic effect in our patients treated with Sertraline because 70% of the treated subjects suffer from a severe episode of depression, 14% serious, 4% moderate, and 12% mild episode (Figure 2). A complete remission of the treated Sertalin was not achieved by any respondent. The most common side effects of SSRI are gastrointestinal problems, headache and tremor. The evaluation revealed several side effects associated with the treatment of Flusetine in the treatment of other SSRI antidepressants. Flusetin, by other authors, may, however, be the first choice among medication for patients with rapid antidepressant effect (Mackay et al., 1997; Mather et al., 2002).

Continuous treatment SSRI with antidepressants and regular visit to psychiatrist or family doctor during an acute phase is associated with a significant reduction of recidivism or the recurrence of depression. Supervision and counseling of a pharmacist during this period can be invaluable (24). Clinicians should focus on suppressing of recidivism with long-term pharmacotherapy treatment of antidepressants with a combined psycho treatment which improves treatment outcomes, especially at patients with high risk of relapse (21).

Conclusion

Our respondents who are treated with the most prescribed SSRI antidepressants (Paroxetin, Sertalin, Flusetin) generally have poor treatment outcome, and despite treatment in the first 6 months they suffer from relapses of depressive symptoms and a very serious level of suicide.The most difficult remission of symptoms of depressive episode has been achieved by treatment of the most commonly recommended and used Paroxetine and Sertaline. Sertalin is solely responsible for suicide intentions in the first 6 months of treatment with a prevalence rate of 12%. It seems appropriate to control the adherence of SSRI antidepressants and improving pharmacotherapy with psychotherapy.

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Abstract

In this paper the instructions for preparing camera ready paper for the Journal are given. The recommended, but not limited text processor is Microsoft Word. Insert an abstract of 50-100 words, giving a brief account of the most relevant aspects of the paper. It is recommended to use up to 5 key words.

Key words: Camera ready paper, Journal.

Introduction

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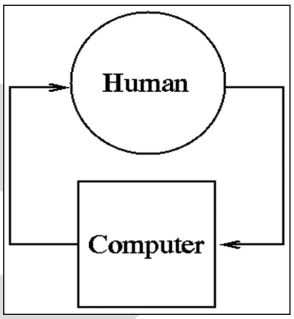

Figure 1. Text here

Conclusion

Be brief and give most important conclusion from your paper. Do not use equations and figures here.

Acknowledgements (If any)

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