

COMORBIDITIES IN ALCOHOL USE DISORDERS IN TUZLA CANTON AREA - BOSNIA AND HERZEGOVINA

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SUMMARY

Introduction: Previous research has shown the simultaneous presence of health diseases and alcohol use disorder (AUD). This research emphasizes the importance of individual diseases, the simultaneous presence and connection of different diseases, which creates the conditions for more adequate treatment of patients with AUD. Determine somatic, neurological and psychiatric diseases in patients with AUD in the Tuzla Canton (TK) in the period from 01.01.2011. to 31.12.2015.

Subjects and methods: A retrospective study on the systematic cause of 1,863 patients with AUD recorded in the TK health system.

Results: Among 1004 (53.9%) patients with AUD, somatic diseases were present; in men: arterial hypertension 573 (31.7%), alcoholic liver disease 269 (14.9%), diabetes mellitus 211 (11.7%); and in women: arterial hypertension 27 (49.1%), diabetes mellitus 27 (49.1%), elevated lipoproteins 3 (5.5%); alcoholic liver disease 1 (1.8%) and anemia 1 (1.8%). Among 1196 (64.2%) patients with AUD, neurological diseases were present; in men: cognitive impairment 627 (34.7%), post-stroke condition 418 (23.1%), polyneuropathy 269 (14.9%); and in women, post stroke condition 28 (50.9%). Psychiatric comorbidity was determined in 1619 (86.9%) patients with AUD; in men: depressive disorder 806 (44.6%), personality disorder 660 (36.5%), while nicotine addiction 27 (1.5%) and dementia 13 (0.7%) were least present; in women: personality disorder 33 (60.0%), neurotic disorder 27 (49.1%), depressive disorder 22 (40.0%). The largest number of patients with somatic (787 or 42.25%), neurological (939 or 50.40%) and psychiatric comorbidity (939 or 50.40%) belonged to the age group 55-64.9 years.

Conclusion: Slightly more than half of the patients with AUD were diagnosed with somatic diseases, almost two thirds were diagnosed with neurological diseases and with more than four fifths of patients were diagnosed with psychiatric diseases. Of the somatic diseases the most common ones were, arterial hypertension, diabetes mellitus, and alcoholic liver disease; from neurological diseases: cognitive impairment, post-stroke condition and polyneuropathy; and the most common of psychiatric illnesses were depressive disorder and personality disorder. The largest number of patients are in the ages of 55-64.9.

Key words: medical characteristics - alcohol use disorder - Bosnia and Herzegovina

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INTRODUCTION

Research on alcohol-induced disorders in the general population is conducted based on the amount of alcohol sold per capita, the number of hospitalized alcoholics, the number of alcohol intoxications, and the mortality of alcoholics due to liver cirrhosis (Thaller 2002). Also there are interests in research of social factors and their impact on alcohol use disorder in the context of the status and conditions in which people live in relation to: age, sex, marital status, level of education, municipality of residence, home ownership status, family structure, employment status, and monthly monetary income (Mešanović et al. 2020a) and personality of the alcoholic through seven perspectives (Mešanović et al. 2020b). Chronic alcohol abuse and alcohol addiction are often associated with various somatic disorders that may be directly related to alcohol toxicity (Sinanović 2012). As a part of alcoholism, numerous neurological, psychiatric and internal syndromes occur. The most common neurological syndromes are polyneuropathy, alcoholic tremor, syncope and Wernicke's encephalopathy (Sinanović 2010). Drinking alcohol is also a significant cause of somatic diseases. In the United Kingdom, about 15-30% of men and 8-15% of women admitted to general hospitals in urban areas have

alcohol-related problems, while the percentage in America is higher at 20-40% (Thaller 2002). Jocelyn (2014) states that subacute and chronic alcohol consumption can have clinical consequences in the form of alcoholic liver disease, liver cirrhosis, atrial fibrillation, cardiomyopathy, gastrointestinal cancer, neuropathy, pancreatitis, thrombocytopenia, and anemia. According to some research, two thirds of all liver cirrhosis is conditioned by alcohol, while the prevalence of liver cirrhosis in alcoholics ranges from 5-6% (Sinanović 2010). A meta-analysis that analyzed potential modifiers of the connectivity effect and examined the differential effects of alcohol consumption by anatomical location and stage of cancer, provided evidence of the relationship, in the form of a letter "J", between alcohol consumption and the risk of colon cancer. (McNabb et al. 2020). Liver cirrhosis-related deaths in European countries vary significantly, from a high 54.8 cirrhosis-induced deaths per 100,000 inhabitants in Hungary to a low 2.9 per 100,000 inhabitants in Ireland (Thaller 2002). It is estimated that an increase in alcohol consumption of a liter per capita causes an increase in mortality from liver cirrhosis by an additional 3-4 / 100,000 for men and 1/100,000 for women (Ramstedt 2007). Basra and Anand (2011) point out that 70% of patients with alcoholic hepatitis will develop liver cirrhosis. Acute

and chronic alcohol consumption is associated with cardiac arrhythmias, especially atrial fibrillation (Balbão et al. 2009), where excessive chronic alcohol consumption has a destructive role on cardiac tissue, which significantly worsens rhythm and contractile activity, and is manifested by the appearance of cardiac arrhythmias and dilated cardiomyopathy. The most common type of arrhythmia is permanent atrial fibrillation (61%). Paroxysmal atrial fibrillation and supraventricular extrasystoles were found in patients without significant echocardiographic changes. These arrhythmias occurred after excessive alcohol consumption. Paroxysmal atrial fibrillation is converted to a normal sinus rhythm after a short period of abstinence or after pharmacological therapy. Ventricular arrhythmias were rare (ventricular extrasystoles, permanent ventricular tachycardia 4.7%, Torsada de point 1.5%). Conduction disorder (left branch block-LBBB 6.3%, right branch block - RBBB 10%) was found in patients who consumed > 150 g/day of alcohol for > 10 years, with dilated ventricles and significantly impaired systolic ventricular function (Krasniqi et al. 2013). Alcohol-induced cardiovascular disease has a complex multigenic etiology. Sudden cardiac death is a known occurrence of alcoholism that may be associated with the arrhythmogenic effect of alcohol. In addition to the increased risk of cardiomyopathy, chronic alcohol consumption is associated with an increased risk of dementia, the development of liver or pancreatic insufficiency, and oral and pharyngeal cancer (Laurent and Edwards 2014). The key features of alcoholic cardiomyopathy are cardiac hypertrophy and ventricular dilatation, and the disease manifests itself mainly as cardiomegaly, congestive heart failure, and even cardiac death (Leibing & Meyer 2016).

Acetaldehyde is formed in the process of ethanol metabolism and has direct carcinogenic and mutagenic effects by modifying DNA. A meta-study showed an association of a functional genetic variant of alcohol metabolites with an increased risk of esophageal and gastric cancer. The greatest increase in the risk of malignancy was recorded in the upper digestive tract (oral cavity, pharynx, larynx) and esophagus (squamous cell carcinoma), weaker correlations were associated with gastric, pancreatic and colorectal neoplasia (Haas et al. 2012). Alcoholic neuropathy is a nerve damage that occurs due to long-term excessive alcohol consumption and is characterized by spontaneous pain. Chronic alcohol consumption causes painful peripheral neuropathy for which there is no reliable successful therapy. The mechanism of alcoholic neuropathy is not well known, but several explanations have been proposed. This includes the activation of microglia after chronic alcohol consumption, oxidative stress that leads to nerve damage by free radicals. Nutritional deficiency (especially thiamine deficiency) and / or direct toxic effects of alcohol are also responsible in alcohol-induced neuropathic pain. Treatment is aimed at stopping

further damage to peripheral nerves and restoring normal function. This can be achieved by abstinence from alcohol and a nutritionally balanced diet that involves vitamin B intake (Chopra & Tiwari 2012). The prevalence of polyneuropathy in research varies significantly. The overall prevalence of polyneuropathy in the general population appears to be about 1% and increases to 7% among the elderly. Polyneuropathy seemed to be more common in Western countries than in developing countries and there are indications that women are affected more often than men. Risk factor profiles vary from country to country. In developing countries, infectious diseases are more common causes of neuropathy, while in Western countries, in particular, diabetes, alcohol abuse, cytostatic drugs, and cardiovascular disease are most commonly associated with polyneuropathy. Polyneuropathy has been reported to exist in 13–66% of chronic alcoholics, depending on the diagnostic criteria for diagnosing neuropathy. It is estimated that the risk of developing polyneuropathy in chronic alcoholics is 3.9 times higher. Treatment other than cessation of alcohol consumption and improvement in dietary intake is symptomatic (Hanewinkel et al. 2016). The most common hematological abnormalities in alcoholism are increased average corpuscular volume of erythrocytes and thrombocytopenia. The etiology is multifactorial, including malnutrition with folate deficiency, direct alcohol toxicity, and sequestration in an enlarged spleen. Sideroblastic anemia caused by the harmful effects of alcohol on pyridoxine metabolism occurs due to hemolytic anemia caused by hypersplenism and megaloblastic anemia. Leukopenia can be seen and is probably caused by the direct toxic effect of alcohol on the bone marrow (Homann & Hasselbalch 1992). Thrombocytopenia in chronic alcoholics can be caused by splenomegaly, folate deficiency, and, most commonly, the direct toxic effect of alcohol on production, survival time, and platelet function. Platelet counts begin to rise after two to five days of abstinence from alcohol. The condition of thrombocytopenia is benign, and clinically significant bleeding is rare (Peltz 1991). An epidemiological study of the prevalence of alcohol use disorders (AUD) and mental health disorders (MHD) found that 43.9% of individuals with lifelong AUD had at least one lifelong MHD, and 17.9% of subjects with lifelong MHD had lifelong AUD. For most comorbidity combinations, MHD preceded the onset of AUD (Glantz et al. 2020). Alcohol is most often abused as a means of alleviating anxiety, depression and insomnia (self-medication hypothesis) which can result in alcohol abuse and addiction and worsening of anxiety and depressive symptoms until clear secondary psychiatric disorders appear (Buljan 2012). Major depression and alcohol-related disorders often occur at the same time. The severity of depression depends on the size and duration of comorbid AUD, with serious implications for disease prognosis (Riga et al. 2020). In studies

conducted in Croatia, the comorbidity of alcoholism with opiate addiction is 12-65%, with schizophrenia 13%, with anxiety disorders 6-20%, and with post-traumatic stress disorder (PTSD) 61.6% (Kozarić-Kovačić 2009). Marić (2005) states that the comorbidity of mental illness with alcoholism in Serbia occurs in 76% men and 65% women and the most common ones are personality disorder, anxiety disorder and depression. While Buljan (2012) states disorders caused by other means of addiction as the most common comorbid psychiatric disorders 18%, antisocial personality disorder 14.4%, mood disorder 13.4%, anxiety disorder 9.4% and schizophrenia 3.8%. About 37% of alcohol addicts experience comorbidity with other mental disorders and when the abuse and dependence on illegal drugs is added, about 86% of women and 78% of men addicted to alcohol experience comorbidity with other mental disorders. (Buljan 2012). A study examining patterns of comorbidities between PTSD and depression, other anxiety disorders, and alcohol-related disorders found that diagnoses of depression, other anxiety disorders, and alcohol-related disorders were more prevalent in people with PTSD than in those without PTSD. And; depression was found in 34% of people with PTSD, while alcohol-related disorders were reported in 7% (de Castro Longo et al. 2020). Hasanović and Pajević (2012) state the fact that secondary alcoholism, in the form of self-medication with alcohol, is especially pronounced in veterans with PTSD in Bosnia and Herzegovina. A study conducted in Bosnia and Herzegovina found that the most common somatic comorbid diseases in alcoholics were diseases of the gastrointestinal system, present in 37.9% of patients and neurological diseases with 33.3%. Of the mental comorbidities, the most common was anxiety disorder 72.7%, while depressive disorder was present in 53.1% of alcoholics. In addition to neurotic disorders, psychotic decompensations were less common in alcoholics 17.4% as well as personality disorders 17.4% (Petrov et al. 2012). A study conducted at the Psychiatric Hospital Sarajevo during one calendar year determined the comorbidity of post-traumatic stress disorder and permanent personality changes after catastrophic experiences with alcoholism in 58.3% of men (Begić 2017). A study on the somatic comorbidity of alcoholism conducted at the Clinic of Psychiatry in Tuzla in the period 2007-2010. showed that somatic comorbidity was present in 59.4% of subjects. The most common comorbid conditions were brain disease with cognitive impairment 13%, high blood pressure 11.8%, polyneuropathy 10.6%, heart disease 9.3%, metabolic syndrome 6.9%, endocrine disease 5.4%, pancreatic disease and crisis of consciousness 3.6% (Šakušić et al. 2012). The first scientific research on the prevalence of alcoholism and smoking in Bosnia and Herzegovina was published in the period from 1962 to 1977 (Mehić-Basara et al. 2007). The first epidemiological research on alcoholism in the Tuzla region

was done by Omer Mijatov in 1980 and was published in a book titled "Alcoholism in the Tuzla Region".

The reason for researching the medical characteristics of alcoholism in Tuzla Canton (TK) is an attempt to show the current state of the problem, the impact of medical factors on the problem of alcoholism, to develop a new strategy for prevention and treatment of alcoholism in TK and to create a basis for further research in the field of alcoholism.

The aim of the research is to determine the distribution of medical characteristics of alcoholism in the area of Tuzla Canton in the period from 01.01.2011. to 31.12.2015. years in relation to: somatic, neurological and psychiatric diseases in comorbidity, hospitalization, number and length of hospitalizations.

SUBJECTS AND METHODS

A retrospective study was conducted on the systematic cause of 1,863 patients with the problem of alcoholism recorded in the health system in the area of Tuzla Canton in the period 01.01.2011. - 31.12.2015. years. The study included persons of both sexes, of all ages, who according to the diagnostic criteria of the International Classification of Diseases - 10 revisions (ICD-10) belong to the codes F10.0-F10.9. The collected data were statistically processed, Student's t-test was used to compare the values of continuous variables between groups, and the Hi-square test was used to compare categorical variables. The statistical significance of the difference in results was set at the level of $p < 0.05$

RESULTS

The largest number of patients, more than four fifths, were on outpatient treatment. Less than a fifth of the men and less than a dozen women in the sample were hospitalized. Among men in the sample there is a statistically significant difference in distribution in relation to the type of treatment ($\chi^2=789.3$; $p < 0.001$) and among women ($\chi^2=32.0$; $p < 0.001$). The distribution of patients in relation to the type of treatment between the sexes shows a statistically significant difference in level ($p < 0.001$) (Table 1). In the sample, the hospital treatment was conducted among 313 patients, to which the largest number of men, slightly more than one half had one hospitalization, one quarter had two hospitalizations, less than one tenth had three hospitalizations, while 0.6% had seven hospitalizations. One third of the women were hospitalized with one, two and three hospitalizations. Among the examined men, there is a statistically highly significant difference in the distribution in relation to the number of hospitalizations ($\chi^2=557.8$; $p < 0.001$), while among women there is no statistically significant difference ($\chi^2=4.67$; $p=0.32$). The distribution of respondents in relation to the number of hospitalizations between the sexes is on the verge of a statistically significant difference ($\chi^2=18.70$; $p=0.05$) (Table 2).

Table 1. Distribution of treated patients with alcoholism problem in the area Tuzla Canton by type of treatment in relation to gender

Type of treatment	Men		Women		In total		χ^2 - test	p
	N	%	N	%	N	%		
Hospitalized	310	17.10	3	5.50	313	16.80	821.35	<0.001
Outpatient	1498	82.90	55	94.50	1550	83.20		
In total	1808	100	55	100	1863	100		

χ^2 - Chi square test; p - the degree of significance of the difference in results

Table 2. Distribution of treated patients with alcoholism problem in the area Tuzla Canton according to the number of hospitalizations in relation to gender

Number of hospitalizations	Men		Women		In total		χ^2 - test	p
	N	%	N	%	N	%		
One	177	57.10	1	33.33	178	56.90	18.70	0.05
Two	80	25.80	1	33.33	81	25.90		
Three	26	8.40	1	33.33	27	8.60		
Four	16	5.20	-	-	16	5.10		
Five	5	1.60	-	-	5	1.60		
Six	4	1.30	-	-	4	1.30		
Seven	2	0.60	-	-	2	0.60		
In total	310	100	3	100	313	100		

χ^2 - Chi square test; p - the degree of significance of the difference in results

Table 3. Distribution of treated patients with alcoholism problem in the area Tuzla Canton according to somatic diseases and in relation to gender

Somatic diseases	Men		Women		In total		χ^2 - test	p
	N	%	N	%	N	%		
Doesn't exist	836	46.20	23	41.80	859	46.10	5906.97	<0.001
Arterial hypertension	388	21.50	-	-	388	20.80		
Alcoholic liver disease	270	14.90	1	1.80	271	14.50		
Arterial hypertension + Diabetes mellitus	160	8.80	27	49.10	187	10.00		
Elevated lipoproteins	28	1.50	3	5.50	31	1.70		
Diabetes mellitus	27	1.50	-	-	27	1.40		
Chronic bronchitis	23	1.30	-	-	23	1.20		
Arterial hypertension + diabetes mellitus + elevated lipoproteins	19	1.10	-	-	19	1.00		
Anemia	14	0.80	1	1.80	15	0.80		
Malignant diseases	14	0.80	-	-	14	0.80		
Alcoholic stomach disease	11	0.60	-	-	11	0.60		
Heart disease	10	0.60	-	-	10	0.50		
Alcoholic disease of the liver and pancreas + arterial hypertension + diabetes mellitus	6	0.30	-	-	6	0.30		
Alcoholic disease of the pancreas	2	0.10	-	-	2	0.10		
In total	1808	100	55	100	1863	100		

χ^2 - Chi square test; p - the degree of significance of the difference in results

Somatic diseases

Slightly more than half of the men in the sample had somatic diseases in comorbidity. Most men had arterial hypertension, over 31% of them, almost 15% had alcoholic liver disease, and almost 12% had diabetes mellitus. Slightly less than half of the women had arte-

rial hypertension and diabetes mellitus; alcoholic liver disease and anemia accounted for 1.8%. Among the examined men ($\chi^2=5711.9$; $p<0.001$) as well as women ($\chi^2=104.2$; $p<0.001$) there is a statistically highly significant difference in the distribution of somatic diseases. The distribution of subjects in relation to somatic diseases between the sexes shows a statistically

significant difference ($p < 0.001$) (Table 3). The largest number of patients with somatic comorbidity, slightly less than half, belonged to the age group 55-64.9. Slightly less than one-fifth of patients in the age group 45-54.9 had alcoholic liver disease, diabetes mellitus, and elevated arterial blood pressure. The distribution of somatic diseases in relation to age groups shows a statistically significant difference ($\chi^2 = 1639.1$; $p < 0.001$) (Table 4).

Neurological diseases

In our study, two-thirds of patients had neurological diseases in comorbidity. One-third of men had cognitive impairment; condition after stroke 23.1%, polyneuropathy 14.9%, the least present was Parkinson's disease with 0.2%. Slightly more than half of the women had a post-stroke condition, while slightly less than half did not have a persistent neurological disease in comorbidity. There was a statistically significant difference in the distribution of neurological diseases among the examined men ($\chi^2 = 2272.5$; $p < 0.001$), and among women ($\chi^2 = 35.6$; $p < 0.001$). The distribution of neurological diseases between the sexes shows a statistically significant difference ($p < 0.001$) (Table 5). More than half of the patients in the sample with neurological disorders in comorbidity belonged to the age group 55-64.9; and within this group, neurological comorbidity was slightly less than 70%; less than a third had cognitive impairment

and post-stroke condition, while polyneuropathy was the least present 0.5%. The distribution of neurological diseases in relation to age groups shows a statistically significant difference ($p < 0.001$) (Table 6).

Psychiatric illness

The largest number of patients in the sample, slightly less than half, had a depressive disorder due to psychiatric comorbidity. Most men, slightly less than half, had depressive disorder; third-person personality disorder, while nicotine addiction 1.5% and dementia 0.7% were least present. Among women, the largest number, slightly less than two thirds had a personality disorder, about half had a neurotic disorder and slightly more than one third had a depressive disorder. There was a statistically significant difference in the distribution of psychiatric illnesses among the examined men ($\chi^2 = 1479.9$; $p < 0.001$), and among women ($\chi^2 = 106.5$; $p < 0.001$). The distribution of psychiatric illnesses between the sexes shows a statistically significant difference ($p < 0.001$) (Table 7). The largest number, half of the respondents, belonged to the age group 55-64.9; where almost half within the group had a depressive disorder, one third had a personality disorder, while the least prevalent were neurotic disorder 12.6% and dementia at almost 1%. The distribution of psychiatric diseases in relation to age groups shows a statistically significant difference ($p < 0.001$) (Table 8).

Table 4. Distribution of treated patients with alcoholism problem in the area Tuzla Canton according to somatic diseases in relation to age groups

Somatic diseases	25-34.9 g.		35-44.9 g.		45-54.9 g.		55-64.9 g.		65-70 g.		χ^2 - test	p
	N	%	N	%	N	%	N	%	N	%		
Doesn't exist	12	0.64	57	3.06	184	9.88	446	3.94	173	9.29	1639.13	<0.001
Arterial hypertension	26	1.40	27	1.45	215	1.54	114	6.12	30	1.61		
Alcoholic liver disease	2	0.11	8	0.43	110	5.90	92	4.94	41	2.20		
Arterial hypertension + Diabetes mellitus	-	-	15	0.80	47	2.52	79	4.24	53	2.84		
Elevated lipoproteins	2	0.11	3	1.64	8	0.43	9	0.48	4	0.21		
Diabetes mellitus	-	-	-	-	1	0.05	14	0.75	2	0.11		
Chronic bronchitis	2	0.11	-	-	9	0.48	7	0.38	1	0.05		
Arterial hypertension + diabetes mellitus + elevated lipoproteins	-	-	-	-	3	1.64	6	0.32	5	2.73		
Anemia	2	0.11	3	1.64	2	0.11	6	0.32	-	-		
Malignant diseases	-	-	-	-	5	0.27	3	1.64	3	1.64		
Alcoholic stomach disease	1	0.05	3	1.64	4	0.21	1	0.05	1	0.05		
Heart disease	2	0.11	-	-	4	0.21	6	0.32	4	0.21		
Alcoholic disease of the liver and pancreas + arterial hypertension + diabetes mellitus	-	-	-	-	-	-	4	0.21	-	-		
Alcoholic disease of the pancreas	-	-	-	-	2	0.11	-	-	-	-		
In total	49	2.63	116	6.22	594	31.88	787	52.25	317	7.02		

χ^2 - Chi square test; p - the degree of significance of the difference in results

Table 5. Distribution of treated patients with alcoholism problem in the area Tuzla Canton according to neurological diseases and in relation to gender

Neurological diseases	Men		Women		In total		χ^2 - test	p
	N	%	N	%	N	%		
Doesn't exist	641	35.50	26	47.30	667	35.80	1586.13	<0.001
Cognitive impairment	497	27.50	-	-	497	26.70		
Post-stroke condition	261	14.40	28	50.90	289	15.50		
Polyneuropathy	223	12.30	-	-	223	12.00		
Post-stroke condition + cognitive impairment	111	6.10	-	-	111	6.00		
Post stroke condition + polyneuropathy	28	1.50	-	-	28	1.50		
Crisis of consciousness	24	1.30	1	1.80	25	1.30		
Post-stroke condition + cognitive impairment + polyneuropathy	20	1.10	-	-	20	1.10		
Parkinson's disease	3	0.20	-	-	3	0.20		
In total	1808	100	55	100	1863	100		

χ^2 - Chi square test; p - the degree of significance of the difference in results

Table 6. Distribution of treated patients with alcoholism problem in the area Tuzla Canton according to neurological diseases in relation to age groups

Neurological diseases	25-34.9 g.		35-44.9 g.		45-54.9 g.		55-64.9 g.		65-70 g.		χ^2 - test	p
	N	%	N	%	N	%	N	%	N	%		
Doesn't exist	11	0.59	21	1.13	208	11.16	289	15.51	136	9.29	1639.12	<0.001
Cognitive impairment	-	-	1	0.05	133	7.14	280	15.03	83	1.61		
Post-stroke condition	-	-	1	0.05	31	1.66	194	10.41	63	2.20		
Polyneuropathy	-	-	1	0.05	118	6.33	86	4.61	18	2.84		
Post-stroke condition + cognitive impairment	-	-	-	-	42	2.25	63	3.38	6	1.64		
Post-stroke condition + polyneuropathy	-	-	1	0.05	28	1.50	13	0.70	1	0.05		
Crisis of consciousness	1	0.05	1	0.05	5	0.27	12	0.64	6	0.21		
Post-stroke condition + cognitive impairment + polyneuropathy	-	-	-	-	3	0.16	-	-	-	-		
Parkinson's disease	-	-	-	-	-	-	2	0.11	1	0.05		
In total	12	0.64	25	1.34	568	30.49	939	50.40	317	7.02		

χ^2 - Chi square test; p - the degree of significance of the difference in results

DISCUSSION

The results of the research showed that the treatment of alcoholism in the area of TK is mostly performed by outpatient treatment. According to the results of the research, at the Clinic for Psychiatry of the University Medical Center in Tuzla in the period 2011-2015 due to alcoholism, a total of 599 first and/or repeated admissions were made. There were 119.8±2.3 admissions per year or 9.31±1.8 monthly admissions; where the largest number of hospitalizations was realized during the months: July, November and December, which is in line with the previous study (Delic et al. 2010). The average duration of hospital treatment of patients in the sample was 16.99±6.80 days; where the longest hospitalization was 32 days. Women were hospitalized for a shorter time 12.67±8.1 days compared to men 17.03±6.81 days. The

total length of hospitalization at the Clinic for Psychiatry of the University Medical Center in Tuzla in the period from 2011 to 2015 due to alcoholism is 5,251 days, multiplied by 138.6 KM, which costs one day of hospitalization (stay and basic laboratory tests), the amount of 728,000 KM shows how much the budget of Tuzla Canton spends on the treatment of alcoholism in the observed five years. This amount does not include the cost of services, additional diagnostic procedures and medications, which further increases the cost of treatment to about one million convertible marks. Compared with Mijatov's previous study (1980), in which the average length of hospital treatment was 26.7 days, the average duration of hospital treatment was reduced by 10 days. Mijatov (1980) in his research states that about 40% of treated alcoholics underwent hospital treatment while our research shows that 16.8% of treated

Table 7. Distribution of treated patients with alcoholism problem in the area Tuzla Canton according to psychiatric diseases and in relation to gender

Psychiatric diseases	Men		Women		In total		χ^2 - test	p
	N	%	N	%	N	%		
Doesn't exist	242	13.50	-	-	244	13.10	1586.13	<0.001
Depressive disorder	532	29.40	21	38.20	553	29.70		
Personality disorder	284	15.70	5	9.10	289	15.50		
Depressive disorder + personality disorder	226	12.50	1	1.80	227	12.20		
Neurotic disorders	202	11.20	1	1.80	203	10.90		
Neurotic disorders + personality disorder	93	5.10	26	47.30	119	6.40		
Psychotic disorder	81	4.50	-	-	81	4.30		
Psychotic disorder + personality disorder	57	3.20	1	1.80	58	3.10		
Psychotic disorder + depressive disorder	49	2.70	-	-	49	2.60		
Nicotine addiction	27	1.50	-	-	27	1.40		
Dementia	13	0.70	-	-	13	0.70		
In total	1808	100	55	100	1863	100		

χ^2 - Chi square test; p - the degree of significance of the difference in results

Table 8. Distribution of treated patients with alcoholism problem in the area Tuzla Canton according to psychiatric diseases in relation to age groups

Psychiatric diseases	25-34.9 g.		35-44.9 g.		45-54.9 g.		55-64.9 g.		65-70 g.		χ^2 - test	p
	N	%	N	%	N	%	N	%	N	%		
Doesn't exist	2	0.11	1	0.05	67	3.60	102	5.48	71	3.81	467.11	<0.001
Depressive disorder	2	0.11	2	0.11	202	10.84	306	16.43	41	2.20		
Personality disorder	5	0.27	6	0.05	71	3.81	186	9.98	20	1.07		
Depressive disorder + personality disorder	2	0.11	5	0.05	102	5.48	88	4.72	30	1.61		
Neurotic disorders	-	-	3	0.16	27	1.45	105	5.64	68	3.65		
Neurotic disorders + personality disorder	-	-	-	-	53	2.84	13	0.70	53	2.84		
Psychotic disorder	-	-	2	0.11	14	0.75	48	2.58	17	0.91		
Psychotic disorder + personality disorder	1	0.05	4	0.21	13	0.70	35	1.88	5	0.27		
Psychotic disorder + depressive disorder	-	-	1	0.05	9	0.48	34	1.83	5	0.27		
Nicotine addiction	-	-	1	0.05	8	0.43	13	0.70	5	0.27		
Dementia	-	-	-	-	2	0.11	9	0.48	2	0.11		
In total	12	0.64	25	1.34	568	30.49	939	50.40	317	7.02		

χ^2 - Chi square test; p - the degree of significance of the difference in results

alcoholics underwent hospital treatment. The results of the research are in line with previous research that indicates a tendency to reduce the total number of psychiatric hospitalizations, as well as a decrease in the number of hospitalizations diagnosed with alcoholism (Ćatipović et al. 2014, Ljubičić & Ljuban 2007).

The results of our research indicate that the average number of hospitalizations per admitted patient in the sample is 1.7 ± 0.9 hospitalizations, and is lower than the results of European studies which amount to 4.9 ± 0.5 hospitalizations (Bardazzi et al. 2017); while the average length of hospitalization is 16.7 ± 1.5 days and is

higher than the results of European research, which is 8.5 ± 1.2 days (Bardazzi et al. 2017). A study of alcoholism conducted in Europe states that the establishment of abstinence and moderate alcohol consumption are associated with fewer hospitalizations and fewer sick days, ie shorter length of hospitalization per respondent (Miquel et al. 2017), while stronger alcohol consumption is associated with higher hospital treatment costs which belongs to the direct costs, with a share of 57% in the total costs of alcoholism treatment in Europe (Kline-Simon et al. 2014). The cost of alcohol dependence in Europe is € 1,591-7,702 per patient, including direct and

indirect costs (Laramee et al. 2013). In this study, the cost of hospital treatment (direct cost) in Tuzla Canton is 1215.35 convertible marks or 623.25 euros per hospitalization, which is 31% less than the total cost of treatment in Europe and this difference would correspond to the indirect cost, which could not be determined, therefore the costs of treatment in Tuzla Canton would be the same as the costs of treatment in Europe. The results of the research determined that in the largest number of patients with AUD, the presence of somatic diseases was 53.9%, and the most frequently recorded was high arterial blood pressure 32.2% and alcoholic liver disease 14.5%. The obtained results are in accordance with the research conducted at the Clinic for Psychiatry of the University Medical Center Tuzla, which found that in patients treated for alcoholism, somatic diseases are present in 59.4% of respondents; where elevated blood pressure is represented by 11.8%, and alcoholic liver disease by 14.3% (Šakušić et al. 2012). In a study conducted in Croatia, somatic diseases in alcoholics were present in 71% of respondents, with the most common alcoholic liver disease with 56%, in a high percentage compared to European studies showing the presence of alcoholic liver disease in 19.6% of alcoholics. (Lesica et al. 2010). Research in Ireland found a higher predisposition of female alcoholics to develop alcoholic liver disease (Nielsen et al. 2017) Studies conducted in Hungary have indicated a high presence of somatic diseases in psychiatric patients at 73% (Mora & Peter 2016), while the presence of somatic diseases in alcoholics is between 7.6% in France (Nabukpo et al. 2016) and 61.7% in Germany (Salize et al. 2002), namely: cardiovascular diseases 55%; endocrinological diseases 30%, gastroenterological diseases 16% (Mora & Peter 2016), with the most common diseases being alcoholic liver disease 33.7%, hypertension 16.9%, chronic obstructive pulmonary disease 14.1% (Schoepf et al. 2015). Men and women addicted to alcohol have significantly higher risks of a comprehensive spectrum of somatic diseases, both as a disease and as a cause of death, compared to individuals in the general population (Holst et al. 2017). This study determined the presence of neurological diseases in the largest number of patients with AUD, 64.2%, with: cognitive impairment 33.8%, post-stroke condition 24.1% and polyneuropathy 14.6% the most common neurological diseases. The obtained results in comparison with the research conducted at the Clinic for Psychiatry of the University Medical Center Tuzla, Šakušić et al. (2012) found a higher presence of cognitive impairment which in this study was 13%, polyneuropathy 10.6% and consciousness crisis 3.6%. There are several pathophysiological mechanisms of damage to the central and peripheral nervous system by alcohol, which include direct effects through acute intoxication, abstinence syndrome, secondary consequences of eating problems and systemic diseases (Rubino 1992). Alcohol-related cognitive impairment is generally underestimated in clinical

practice, although it could aid in treatment, increase a patient's ability to remain abstinent, and improve therapeutic agreement. Even in the absence of visible neurological complications, excessive and chronic alcohol consumption leads to damage to the structure and function of the brain. The frontocerebellar circle and the Papeza complex, which are involved in motor and executive abilities, are mainly affected. These brain dysfunctions are associated with neuropsychological impairments, including deficits in executive function, short-term memory, social cognition, visual and motor abilities. Such cognitive impairments can interfere with the motivation process to give up harmful patterns of alcohol behavior in favor of healthier lifestyles (such as abstinence or controlled alcohol consumption). They may also limit a patient's ability to fully benefit from treatment (Cabe et al. 2016). Previous studies have shown a complex relationship between alcohol consumption and cognition, but also the process of social and biological aging. The acute effects of alcohol during intoxication are reversible, patients with alcohol dependence and chronic alcohol intake show serious disorders of cognitive functions, especially deficit in executive functions, disorders in problem solving, abstraction, planning, organization and working memory (Weis et al. 2014). Research in the United States indicates that patients with alcohol dependence show more severe cognitive deficits (Levy et al. 2008) in the form of global cognitive impairment and severe executive dysfunction (Spinelli et al. 2017). In addition to cognitive impairment, in 30% of cases after the establishment of abstinence, alcoholic polyneuropathy lags behind as one of the most common neurological consequences of long-term alcohol consumption (Neundörfer et al. 1984). Two studies conducted in Asia, one in China found that low alcohol intake was associated with a reduced risk of stroke and mortality, while heavy alcohol intake was associated with an increased risk of total stroke (Zhang et al. 2014), another study made in Japan indicated a higher risk of hemorrhagic stroke with heavy alcohol use (Iso et al. 2004); while a study done in France demonstrated a greater severity of stroke with heavy alcohol use (Ducroquet et al. 2013). The results of the research determined the presence of psychiatric diseases in 86.9% of the largest number of patients with the problem of alcohol consumption, with depressive disorder 44.5%, personality disorder 37.2% and neurotic disorder 17.3%, the most common psychiatric diseases. A study conducted at the Clinic for Psychiatry of the University Medical Center Tuzla found that psychiatric illnesses are present in 56.9% of patients treated for alcoholism; the most common are: depressive disorder 22.1%, permanent personality changes after catastrophic experiences 9.7%, personality disorders 8.4% (Šakušić et al. 2012). Research conducted in Croatia indicates the presence of psychiatric illnesses in about 37% of patients treated for alcoholism (Buljan 2012); in women, depressive disorder is most often present in

38%, personality disorders in 29%; and in men, post-traumatic stress disorder 13%, depressive disorder 11%, personality disorders 29% (Lesica et al. 2010). The results of a study conducted in Denmark indicate that mental disorders are present in 50.3% of patients treated for alcohol, with the most common being personality disorder 24%, mood disorder 16.8%, drug abuse 16.6% (Flensburg-Madsen et al. 2009), while a study conducted in France found the existence of psychiatric illnesses in 60.9% of patients and in the largest percentage were present depressive disorder 30.6% and personality disorder 26.1% (Nabukpo et al. 2016). The results of research from New Zealand have shown that the existence of alcohol use problems doubles the risk of developing depressive disorder and vice versa. Epidemiological data suggest that the links between them cannot be fully explained by common factors affecting them and that the disorders appear to be causally related. Potential mechanisms underlying these causal relationships include neurophysiological and metabolic changes resulting from alcohol exposure (Boden & Fergusson 2011). There is a high comorbidity of alcohol dependence with mood, anxiety, substance abuse, and personality disorders. In particular, personality disorders are considered significant for contribution and / or as a predisposing factor in the pathogenesis, clinical course and outcome of alcohol dependence treatment. According to clinical and epidemiological studies, the prevalence of personality disorders in alcoholism ranges from as much as 22-40% to as much as 58-78%. The literature focuses primarily on antisocial and borderline personality disorders; however, almost the entire spectrum of personality disorders can be encountered in alcohol dependence, such as addictive, avoidant, paranoid, and others. Many factors, such as sampling methods, diagnostic criteria used, or assessment procedures applied, may explain this large variation (Mellos et al. 2010). At least one personality disorder was present in 40% of alcohol-dependent patients, while that percentage was lower by 16.6% in the general clinical sample. Addictive personality disorders were the most common 13.3%, followed by paranoid and obsessive-compulsive personality disorders (10% each) (Echeburúa et al. 2005). The results of our study are consistent with the study of Gutwinski et al. (2018) who point out that daily alcohol consumption affects the cognitive effects and development of dementia; and that frequent consumption of large amounts of alcohol alters brain functions and reduces cognitive functions. A two-year Chinese study investigated the relationship between alcohol consumption and the risk of dementia in elderly patients diagnosed with a mild cognitive impairment. During this study, 37.5% of patients developed dementia, while heavy drinkers had a higher risk of developing dementia (Xu et al. 2009). This study confirmed the conclusions about the corre-

lation between alcohol and tobacco consumption that he found in his study Zacny (1990), ie. that smokers consume more alcohol compared to non-smokers and alcohol consumers smoke more cigarettes compared to those who do not consume alcohol. A series of studies examining the effects of ethanol on tobacco consumption have shown that ethanol potentiates tobacco consumption and vice versa. The discussion of the possible mechanisms of the connection between the use of alcohol and tobacco includes cross-tolerance between them. The association between alcohol and tobacco consumption may have significance with the problem of their relapse. The combined use of alcohol and tobacco poses a higher risk for the occurrence of comorbid diseases than the sum of the risks of alcohol and tobacco alone (Zacny 1990). The concomitant presence of psychotic disorders with the alcohol use disorder we obtained in this study is consistent with a study conducted by Moggi (2018), which states that about half of patients with schizophrenia develop disorders of psychoactive substance use during their lifetime; of which about one third is AUD. There is no universally valid model of etiology to explain the relationship between psychosis and addiction. The model of self-medication is not empirically confirmed, while for example the model of psychological effects on regulation, the model of vulnerability-stress specific sensitivity to addictive substances due to predisposition to psychosis or the neurobiological common factor of the dopamine regulation dysfunction model in the mesocorticoligical reward system predisposed to primary substance use disorder, has some empirical support. A meta-analysis of the association between alcohol use disorder and major depressive disorder has shown that the presence of any disorder doubles the risks of another disorder, but does not define the nature of this causal relationship (Boden & Fergusson 2011). At the same time, the presence of alcohol use disorders and personality disorders that we found in our research are in line with the research of Boog et al. (2018) whereby in their research they differentiate the most common existence of borderline personality disorder. Borderline personality disorder affects 2.7% of adults. About 78% of adults with borderline personality disorder develop some form of substance use disorder or addiction at some point in their lives (Kienast et al. 2014). Little is known about the role of a wide range of personality disorders in the use of psychoactive substances. The existing literature focuses mainly on antisocial personality disorder and does not draw clear conclusions. A study conducted in the U.S. on 1,174 respondents found alcohol use disorder in 30.1% of respondents. Antisocial, borderline, and schizotypal personality disorders were significantly associated with alcohol use disorders, while narcissistic, schizoid, and obsessive-compulsive personality disorders were of lesser importance (Hasin et al. 2011).

Weaknesses and limitations of the research

A limitation in the research is the fact that we used only data from people who were treated on an outpatient basis in health centers and at the Clinic for Psychiatry, and in hospital only at the Clinic for Psychiatry of UKC Tuzla, which does not represent a true picture of alcoholism in TK. Patients with the problem of alcoholism are also treated at other clinics of the University Medical Center Tuzla due to diseases caused by alcohol consumption without ever being examined at the Clinic for Psychiatry. Given the methodology of this work, we took great care to avoid re-recording the same patients when creating a total sample of the patients we included in the study.

Recommendations for further research

Further research based on the results of this study should be expanded with data on people from the general population, duration of AUD, social status and diseases present at the end of the life of people with AUD; in this way they would have a comprehensive picture of the impact of AUD on an individual's life.

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Contribution of individual authors:

Miralem Mešanović: conception and design of the manuscript, collecting data and statistical procedures, literature searches, analyses and interpretation of data, manuscript preparation and writing the paper;

Izet Pajević: made substantial contributions to conception and design, participated in revising the article and gave final approval of the version to be submitted.

Mevludin Hasanović: made substantial contributions to conception and design, literature searches, statistical analyses and interpretation of data, participated in revising the article and gave final approval of the version to be submitted.

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