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Quality of Life publishes original research papers and reviews and aims to provide a forum for the rapid dissemination of significant novel research in the various disciplines encompassing the Science and technology of food, Public health engineering, Sanitary inspection and control, Environmental and public health. Topics covered by the journal include:

- Dietetics; Nutrition principles applied to foods
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Dear readers and authors,

As Editor-in-Chief of the journal Quality of Life, I look forward to the challenge of creating a journal that will enhance the quality of research in the various disciplines encompassing the Science and technology of food, Public health engineering, Sanitary inspection and control, Environmental and public health in our country, the region as well as at the international level. The journal Quality of Life was registered in the Register of Public Media in 2010 by the Decision of the RS Ministry of Education and Culture. Over the past years, this journal has published a large number of original scientific research papers, communications and review papers. Quality of Life is published twice a year by Pan-European University "Apeiron" Banja Luka. All the papers published so far have undergone a thorough review by the editorial board and the reviewers, made up of experts from both RS/B&H, the surrounding and other countries, from proven and recognized university and research institutions. As a result of a professional approach to selecting and reviewing papers, and raising the quality of the journal, Quality of Life was classified in the first category of journals in 2019 by the Ministry of Education and Culture.

We are proud to say that Quality of Life has been well received by the scientific and the general public in a relatively short period, which gives the editorial board a strong motivation for further work. The editorial team would like to thank our many reviewers who helped to maintain the journal standard; our many authors who submitted their best work to the journal; and, most importantly, our readers for your continuing support. I shall assure all our readers that our consistent efforts will be aimed toward increasing the visibility, impact, editorial cycle time, citations and overall quality of our journals. We very much look forward to strengthening the reputation of our publications, and we want to attract more higher-quality submissions.

In the spirit of continuous improvement, any constructive input on streamlining our processes is very welcome. Please help us grow by citing articles that you read in Quality of Life. We look forward to receiving your contributions in the near future.

Editors

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Original scientific paper

Comparison of Physical and Chemical Composition of Leachate from Three Municipal Waste Landfills: Sarajevo, Zenica and Tuzla (Bosnia and Herzegovina) Case Study

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ABSTRACT: In Bosnia and Herzegovina (BiH), waste management is still based on the preventive disposal of waste in landfills, of which most landfills are unregulated. According to World Bank reports, BiH must deal with the improvement of waste disposal to protect the environment. The aim of this study was to review the physical and chemical composition of leachate from municipal waste landfills. The following standard physicochemical methods were used: pH, total suspended solids (TSS), Biological Oxygen Demand (BOD5), Chemical Oxygen Demand (COD), Total nitrogen (TN), total phosphorus (TP), chlorides, and sulphates. The leachate quality test was conducted over three years at landfills in Sarajevo, Zenica and Tuzla, Bosnia and Herzegovina (BiH). Based on the processed data (from the processed tables), and in comparison with the expected values of pollutants in landfills over the period of 10 years, we can conclude the following: (1) Landfill "Smiljevići" Sarajevo, in the observed period of 3 years, has a higher average value than expected; (2) Landfill "Desetina" Tuzla, in the observed period of 3 years, has a higher average value than expected; (3) Landfill "Mošćanica" Zenica, in the observed period of 3 years, has a higher average value than expected.

Keywords: landfill, leachate, environmental, pollution.

INTRODUCTION

Leachate at the landfill is formed by filtering rainwater or other precipitation through the body of the landfill, during which soluble, colloidal, and suspended solids are separated from the waste (Robinson, 2005). The movement of water through the waste depends on the permeability, porosity, humidity, thickness, chemical migration and internal coatings of the waste, which form impermeable barriers and areas of accumulation in the waste. The amount of water collected layer by the time water saturation is reached indicates the ability of the waste to retain water. In this phase, moisture in the garbage begins to form leachate (Qasim, 1994).

One of the fundamental problems of waste management that landfills face in practice is the collection and treatment of leachate. Their composition and amount of production depend on many factors such as the age of the landfill, type of waste, climatic factors, etc. This wastewater must not be discharged directly into the environment without prior collection and treatment. The composition of leachate changes during the operation of a landfill. These changes mainly depend on the age of the landfill, the type and thickness of the deposited layer of waste, the shape and operation of the landfill and the interaction of leachate with the environment. The composition of leachate is particularly affected by the age of the landfill. As landfills age, the concentration of organic matter decreases more than the concentration of inorganic matter because they decompose and leach, while inorganic matter only leaks. Moisture significantly affects the degree of decomposition of waste, because it facilitates the exchange of substrate and nutrients, dilution of inhibitors and the growth of microorganisms. The way the landfill is built, the way it is disposed, as well as the climate have the most important influence on the moisture content of the landfill. Landfill leachate is a particularly

dangerous pollutant, which can be loaded with heavy metals and various organic and inorganic toxic substances such as pesticides, phenols, dioxins, etc. dissolved from waste. Therefore, these waters must be collected and treated in a controlled manner and their uncontrolled discharge into surface and groundwater without prior treatment must be prevented (Brkanac et al., 2013). In order to ensure long-term stable collection and continuous, economically viable leachate treatment, it is necessary to establish volume control (filtrate production) and a uniform leachate composition. With the strengthening of water quality protection measures and standards, the requirements for leachate treatment have increased significantly (Sang et al., 2006). According to the EU Landfill Directive 1999/31/EC, all water generated during landfill work should be collected and treated before any discharge to the final recipient. Recent research on leachate in municipal landfills shows that these waters are one of the most complex sources of pollution in nature, the composition and quantity of which change significantly during the life cycle of the landfill (Serdarević, 2007).

The production of the filtrate by the decomposition of municipal solid waste from non-hazardous waste landfills changes over time, as waste is decomposed through the following four phases of biodegradation (Toromanović et al., 2021, Qasim, 1994):

- I - The aerobic phase is the initial, short-term phase of decomposition that lasts about a month. At this stage, the decomposition of waste is performed by aerobic bacteria.
- II - The anaerobic, non-methane phase lasts approximately several months. Bacteria that do not need oxygen are active at this stage. The decomposition of waste mainly produces organic acids and alcohols. This phase represents the phase of hydrolysis and acidification.
- III - The anaerobic and unstable phase of methane will last from several months to a year. The chemical structure of the waste is stable; acetate and hydrogen are formed as products.
- IV - Anaerobic stable phase of methane lasts for several years. At this stage, methanogens are active and sensitive to pH. They exist only when the pH is around seven and mainly form CH_4 (methane) and CO_2 (carbon dioxide).
- V – It was additionally introduced as the final phase of waste decomposition. In this phase, some of the upper landfills may have aerobic zones.

Waste management in BiH is still at a low level and is based only on waste disposal in landfills, much of which are unregulated or illegal landfills. Very little research has been done on the impact of landfill water on human health and the environment. So far, a study of leachate management from the Sarajevo landfill has been conducted with a proposal for control and treatment (Serdarevic, 2017). A lot of work has been done on the research of leachate from the Banja Luka landfill (i.e. Markic, 2015), but there is still no significant research from the landfills of Zenica and Tuzla.

The subject of this paper is to monitor the physical and chemical composition of leachate from three landfills in BiH (Sarajevo, Zenica and Tuzla). These landfills are of different "ages", resulting in a different composition of leachate. Values of pollutants in landfills (Sarajevo, Zenica and Tuzla) of over ten years are used to show which results are best regarding the lowest number of parameters that are above the expected value of pollutants in these landfills.

MATERIALS AND METHODS

The subject of this paper is the analysis of leachate quality parameters from landfills in Sarajevo, Zenica and Tuzla in the period from 2016 to 2018.

The regional landfill "Smiljevići" Sarajevo started operating in the 60's of the last century and since 1998 it has been operating as a regional sanitary landfill. The total time of exploitation of this landfill is about 50 years. It covers an area of 65 ha. KJKP "Rad" collects and removes waste from the Sarajevo

Canton. Waste is disposed of at a sanitary landfill, approx. 4.5 km from the city zone. The daily amount of waste in the Sarajevo Canton is approx. 500 tons The selected membrane-biological (MBR) leachate treatment system (2006-2011) did not fully meet the set requirements for discharge treated leachate into a natural watercourse. During its trial operation, the MBR device achieved certain results, especially in certain parameters of leachate load, but from the beginning of the operation, shortcomings in the technical-technological solution were noticed. Due to mechanical failures, the device stopped working after several months of operation. Leachate, untreated and insufficiently purified, was discharged from the Sarajevo landfill into Lepenički potok.

The "Desetine" landfill in Tuzla started operating in 1990, i.e. the total period of waste disposal at this landfill is about 30 years. The sanitary landfill of the city of Tuzla "Desetine" is located in the north-western part of the city. The landfill occupies a total area of approx. 180,000 m^2. "Desetine" landfill was built with a packed impermeable base and a drainage system for controlled drainage of leachate under the body of the landfill. The collected leachate is discharged into the shaft below the dam of the landfill and a special collector together with faecal water and local connections drains into the river Jala, which is about 4 km away. In 2017, households generated about 38,000 tons of mixed municipal waste.

The regional landfill "Mošćanica" Zenica started operating in 2008, and waste has been disposed of at this landfill for about 13 years. The regional landfill "Mošćanica" was built in the northern part of the landfill of the open pit mine "Mošćanica" and now covers an area of 24 ha. The landfill is located 14 km east of the town of Zenica. At the Regional Landfill "Mošćanica", waste is delivered from the area of the region consisting of the City of Zenica and the City of Visoko, and the municipalities of Travnik, Vitez, Busovača, Zavidovići, Žepče, and Novi Travnik. According to statistical data, the region served by the Regional Landfill "Mošćanica" has about 400,000 inhabitants. The amount of waste that was disposed of at this landfill in 2020 amounts to 65,880 tons. A leachate collection and treatment system and a leachate recirculation system have been established at this landfill. The treated leachate from this landfill is discharged into the stream or surface water.

Due to the different ages of landfills in these three local communities, i.e. different ages of estimated waters from the landfill, this paper will deal with the comparison of physical and chemical parameters of leachate from Sarajevo, Zenica, and Tuzla landfills. The analyzed results of leachate monitoring from these landfills in the Federation of BiH were performed by authorized laboratories. The implementation of leachate monitoring is carried out in accordance with the Regulation on the Conditions of Wastewater Discharge into the Environment and the Public Sewerage System (Official Gazette of FBiH 26/20). Physical and chemical parameters analyzed in the leachate from these three landfills are as follows: pH, total suspended solids, BOD_5, COD, total nitrogen (TN), total phosphorus (TP), chlorides, and sulfates.

RESULTS AND DISCUSSION

Table 1 presents the results of the physical and chemical analysis of leachate from the Sarajevo landfill. In 2016 and 2018, pH values were in the range of maximum allowable concentrations (MAC), while in 2017, the values of this parameter were above MAC.

Mean pH value in the period 2016-2018 amounted to 9.11, i.e. slightly higher than MAC or above 9. The total suspended substances in the three-year observation period had values below MAC, i.e. they met the Regulation on the Conditions of Wastewater Discharge into the Environment and the Public Sewerage System , (Official Gazzette of the Federation of BiH, No. 101/15, 1/16, and 101/18). The values of BOD_5 and COD as indicators of an organic load of leachate during the entire monitoring period had far higher values than MAC, i.e., than 25 mg O_2/l and 125 mg O_2/l, respectively. Furthermore, the values of total ni-

trogen (TN) and total phosphorus (TP) had far higher values compared to MAC prescribed by the above Regulation. Chloride and sulphate values were far less than MAC.

Table 1. Results of leachate monitoring from the landfill "Smiljevići" Sarajevo

Date of analysis(year)	2016	2017	2018	Average value	MAC*
pH	8.34	10.21	8.78	9.11	6-9
Total suspended matter (mg/l)	25.3	32.75	15.5	24.52	35
BOD5 (mgO_2/l)	380.4	410.27	851.53	547.40	25
COD (mgO_2/l)	1,290.8	1,555.1	2,818	1,887.97	125
Total nitrogen	142.51	113.09	1,358	537.87	15
Total fosfor (TP) (mg/l)	8.8	3.5	5.26	5.85	2
Chlorides (mg/l)	492.27	759.42	1,422	891.23	3,000
Sulfates (mg/l)	192.1	272.62	479.09	314.60	2,000

** Regulation on the Conditions of Wastewater Discharge into the Environment and the Public Sewerage System (Official Gazette of FBiH 26/20).*

Table 2 also presents the results of the physical and chemical analysis of leachate from the Tuzla municipal waste landfill. The pH values in 2016, 2017, and 2018 were in the range of maximum allowable concentrations, and the average value in this period was 7.52. The total suspended substances had an average value of 23.11 and were also within MAC. BOD_5 and COD values were above the limit values throughout the observation period. The values of total nitrogen were above the limits prescribed by the Regulation, while the values of total phosphorus were within the limits of the MAC. Chlorides in sulphates in the observed period had much lower values compared to those prescribed by the Regulation.

Table 2. Results of leachate monitoring from the landfill "Desetine" Tuzla

Date of analysis(year)	2016	2017	2018	Average value	MAC
pH	7.46	7.61	7.5	7.52	6-9
Total suspended matter (mg/l)	23.5	24.8	21.03	23.11	35
BOD5 (mgO_2/l)	148	95	270	171	25
COD (mgO_2/l)	501	327	840	556	125
Total nitrogen(TN) (mg/l)	220	94.5	646	320.17	15
Total phosphorus (TP) (mg/l)	0.6	0.59	0.75	0.65	2
Chlorides (mg/l)	672	211	820	567.67	3,000
Sulfates (mg/l)	22.3	17.9	56	32.07	2,000
Cu (mg/l)	0.07	0.019	0.018	0.04	
Zn (mg/l)	0.34	0.71	1.84	0.96	
Pb (mg/l)	0.22	0.05	0.13	0.13	
Mg (mg/l)	0.27	0.33	0.75	0.45	
Al (mg/l)	n/d	0.04	0.01	0.03	
Fe (mg/l)	n/d	n/d	4.3	4.3	

** n/d - no data provided*

The data related to the Zenica landfill are presented in Table 3. The pH value in the years of observation, from 2016 to 2018, was within the limits of the Regulation, and its average value is 8.28. The total

suspended substances all these years were above the limits of MAC, especially in 2017, where it was 725 mg/l. BOD_5 was also above the limits prescribed by the Regulation.Only in 2017 that overrun was very small, just 1.9mg/l above the limit. The COD value in 2016 and 2018 was extremely high, while in 2017, it was below the limit. As for the total nitrogen, in 2017, it was 2.83 and was below the limit, and in 2016 and 2017, it was extremely high. The values of total phosphorus have the same data for years as total nitrogen, which means that in 2017 it was below the limit and amounted to 0.26, and in 2016 and 2018, it was above the limits prescribed by the Regulation. In the observed period, the values of chloride and sulfate were extremely low in 2017 and 2018.For 2016 no data were submitted.

Table 3. Results of leachate monitoring from the landfill "Mošćanica" Zenica

Date of analysis (year)	2016	2017	2018	Average value	MAC
pH	8	8.27	8.56	8.28	6 – 9
Total suspended matter (mg/l)	290	725	41	352	35
BOD_5 (mgO_2/l)	463	26.9	682.3	390.73	25
COD (mgO_2/l)	1607	96	2320	1341	125
Total nitrogen(TN) (mg/l)	860.44	2.83	191.56	351.61	15
Total phosphorus (TP) (mg/l)	10	0.26	6.9	5.72	2
Chlorides (mg/l)	n/d	72.3	3119	1595.65	3,000
Sulfates (mg/l)	n/d	189.5	216.8	203.15	2,000
Cu (mg/l)	0.0134	0.001	0.05	0.02	
Zn (mg/l)	0.0287	0.06	0.15	0.08	
Cd (mg/l)	0.003	0.001	0.003	0.002	
Pb (mg/l)	0.0431	0.001	0.08	0.04	

** n/d–no data provided*

Table 4. Comparative presentation of monitoring results (average values per landfill)

Landfill	Smiljevići	Desetine	Mošćanica
pH	9.11	7.52	8.28
Total suspended matter (mg/l)(mg/l)	24.52	23.11	352
BOD_5 (mgO_2/l)	547.4	171	390.73
COD (mgO_2/l)	1887.97	556	1341
Total nitrogen (TN) (mg/l)	537.87	320.17	351.61
Total phosphorus (TP) (mg/l)	5.85	0.65	5.72
Chlorides (mg/l)	891.23	567.67	1595.65
Sulfates (mg/l)	314.6	32.07	203.15
Cu (mg/l)	n/d	0.04	0.02
Zn (mg/l)	n/d	0.96	0.08
Pb (mg/l)	n/d	0.13	0.04
Mg (mg/l)	n/d	0.45	n/d
Al (mg/l)	n/d	0.03	n/d
Fe (mg/l)	n/d	4.3	n/d
Cd (mg/l)	n/d	n/d	0.02

n/d–no data provided

Taking into account the assessment of pollution load caused by wild and locally unregulated solid waste landfills of different ages, in the absence of data on leachate monitoring, garbage composition, and

amount of disposal, when calculating pollution load, for landfills where solid mixed municipal waste is treated for more than 10 years, the composition of leachate is based on the average value of pollutants obtained from the average monitoring results of the Sarajevo landfill "Smiljevići", the landfill "Desetina" Tuzla and the landfill "Mošćanica".

Table 5. Expected value of pollutants inlandfills that are over 10 years old (Institute of Civil Engineering "IG" Banja Luka, 2019).

Parameter	Unit	Value
BOD_5	(mgO_2/l)	280
COD	(mgO_2/l)	1,100
Total suspended matter (mg/l)	(mg/l)	40
Total nitrogen	(mg/l)	300
Total phosphorus	(mg/l)	3
Chlorides	(mg/l)	730
Sulfates	(mg/l)	150
Cu	(mg/l)	0,03
Zn	(mg/l)	1.1
Cd	(mg/l)	0.05
Pb	(mg/l)	0.1
Mg	(mg/l)	0.5
Fe	(mg/l)	3.5
Al	(mg/l)	0.02

Based on the processed data (Tables 1, 2, 3, and 4), and in comparison with the expected values of pollutants in landfills that are over 10 years old (Table 5), we can state the following:

- Landfill "Smiljevići" Sarajevo, in the observed period of 3 years, has a higher average value than expected, namely: BOD5 (mgO2/l) - 547.40, compared to the expected value of 280 (mgO2/l), COD (mg O2/l) - 1887.97 (expected value 1,100). Also, higher than expected values are shown in the presence of Total Nitrogen (TN) (mgN/l) - 537.87 (expected value 300), then Total Phosphorus (TP) (mgP/l) - 5.85, Chlorides (mg/l) - 891.23, Sulfates (mg/l) - 314.60. A lower value than expected was recorded for the total suspended matter - 24.52. As for the other parameters, no data (n/d) were submitted for them.
- Landfill "Desetina" Tuzla, in the observed period of 3 years, has a higher average value than expected, as follows: Total nitrogen (TN) (mgN/l) - 320.17 (expected value 300), Cu (mg/l) - 0.04, Al (mg/l) - 0.03 and Fe (mg/l) - 4.3. In the case of other parameters, a lower value of the parameters than expected was recorded, while no data were submitted for one parameter.
- Landfill "Mošćanica" Zenica, in the observed period of 3 years, has a higher average value than expected, as follows: Total suspended solids - 352, BOD5 (mgO2/l) - 390.73, compared to the expected value of 280 (mgO2/l), COD (mg O2/l) - 1341 (expected value 1,100), Total nitrogen (TN) (mgN/l) - 351.61 (expected value 300), Total phosphorus (TP) (mgP/l) - 5.72, Chlorides (mg/l) - 1595.65 and Sulfates (mg/l) - 203.15. As for the other parameters, they had a lower value than expected, while data for three parameters were not submitted.

Based on all the above, and if we compare these three landfills, the landfill "Desetina" Tuzla had the best results of the analysis, which shows the smallest number of parameters that are above the expected value of pollutants in landfills that are over 10 years old.

For example, the following table 6 shows the results of the analysis, i.e. the physical and chemical parameters of the treated landfill leachate of J.P. Deponija d.o.o. Mostar.

Table 6. Results of physical and chemical analysis "J.P. Deponija d.o.o. Mostar"

Analyzed parameters	Unit of measurement	Analysis results
pH		7.6
Total phosphorus	mg/L	-
Chlorides	mg/L	5.83
Sulfates	mg/L	24.8
Mg	mg/L	230
Fe	mg/L	1713

Based on the results of physical and chemical analysis of "J.P. Deponija d.o.o. Mostar" and the results of the analysis of the three landfills presented in the paper ("Smiljević" Sarajevo,"Desetina" Tuzla,"Mošćanica" Zenica), we can see that the results are within the limits for leachate, which indicates a good treatment process.

CONCLUSIONS

Leachate from sanitary landfills is complex and heavily polluted wastewater. The composition and amount of leachate depends on many factors, which can vary precipitation, size and area of the landfill, type of waste, method of treatment, age of the landfill, etc. Due to the influence of many factors, the composition and amount of leachate vary considerably, which makes it very difficult to choose the appropriate treatment technology.

The only solution for municipal waste landfills is to treat them, but this requires significant material resources in order to comply with EU directives. Also, health and hygienic supervision of wastewater is being done, which, in addition to physical-chemical and toxicological analyzes, also includes a local inspection of the landfill, waste, and wastewater. A local inspection determines the general condition of the landfill and its surroundings. If the landfill meets the conditions of the local inspection, only then will the cleaning begin.

Based on the processed data (Tables 1, 2, 3 and 4), and in comparison with the expected values of pollutants in landfills that are over 10 years old (Table 5), we can conclude the following:

Regarding the landfill "Smiljevići" Sarajevo, in the observed period of 3 years, a total of 8 physical and chemical analyzes were performed, while data for 7 were not submitted. The results tell us that 7 parameters had higher average values than expected, while for only one parameter the value was lower than expected.

In the case of the landfill "Desetina" Tuzla, in the observed period of 3 years, a total of 14 physical and chemical analyzes were performed, while data for 1 were not submitted. The results tell us that for 4 parameters, higher average values were determined than expected, while for 10 parameters the value was lower than expected.

Regarding the landfill "Mošćanica" Zenica, in the observed period of 3 years, a total of 12 physical and chemical analyzes were performed, while data were not submitted for 3. The results tell us that 7 parameters showed higher average values than expected, while for 5 parameters the value was lower than expected.

As a conclusion to all the above, the basic steps in the process of leachate treatment that need to be taken into account are hereby listed again:

- Landfill treatment technology must be applied to reduce leachate production,
- Control of waste transport and disposal at landfills can improve leachate quality,
- The possibility of pre-treatment and connection to the local PTOV or other industrial wastewater treatment plants (if any) as a long-term option is considered/assessed at the site.

Selecting a leachate treatment process is a complex task and requires reliable data for analysis and final selection.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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Original scientific paper

The Treatment of Moderate and Severe Chronic Plaque Psoriasis With Biologics and Biosimilar Drugs

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ABSTRACT: Psoriasis is a chronic, immune-mediated inflammatory skin disease. The condition greatly affects people's quality of life to the extent that it could be life-ruining and stigmatizing. A better understanding of psoriasis pathophysiology allowed the development of targeted therapies, including biologics and biosimilars which are recommended as an option for moderate to severe plaque psoriasis. Our results have shown that administration of biologics (adalimumab and secukinumab) and adalimumab biosimilar led to a significant improvement in the PASI response after 16 weeks. Most patients who have been treated for more than a year have the same PASI response.

Keywords: psoriasis, PASI, biologics, adalimumab, secukinumab, biosimilars.

INTRODUCTION

Psoriasis is a chronic, immune-mediated inflammatory skin disease, consisting of red, scaly plaques occurring most commonly on the elbows, knees, scalp, and lower back, but any skin surface can be affected. Psoriasis affects between 1% and 5% of the population worldwide (Carrascosa et al., 2018).

The condition greatly affects people's quality of life to the extent that it could be life-ruining and stigmatising (Ayala-Fontánez al, 2016). Psoriasis is now considered a systemic disease associated with psychological, metabolic, arthritic, and cardiovascular comorbidities. Approximately 125 million people worldwide have psoriasis. Twelve studies reported the incidence of psoriasis in all ages, with the incidence of the disease varying from 31.4 per 100 000 person-years in Eastern Europe (Russia) to 521.1 per 100 000 person-years in Western Europe (Germany) (Parisi et al., 2020).

Plaque psoriasis is the most common variant of psoriasis. The most rapid advancements addressing plaque psoriasis have been in its pathogenesis, genetics, comorbidities, and biologic treatments. Plaque psoriasis is associated with several comorbidities including psoriatic arthritis, cardiometabolic diseases, and depression (Armstrong & Read, 2020).

In patients with psoriasis, assessing the severity of the disease is an important guideline in deciding whether to treat the patient with local therapy only or with phototherapy and systemic therapy. After the introduction of therapy, the assessment of the severity of the disease is necessary for monitoring the effectiveness of treatment.

Three instruments (scales) are most commonly used to assess the severity of the disease in patients with psoriasis: Psoriasis Area and Severity Index (PASI), Body Surface Area (BSA) and Dermatological Life Quality Index (DLQI) (Oji & Luger, 2015).

PASI is the most commonly used scale to assess skin involvement and clinical severity in patients with psoriasis. In this method, the surface of the affected skin with psoriatic lesions (Area) and the severity of psoriatic lesions (Severity) are evaluated to assess the condition of the disease. Within this score, the degree of redness (Erythema), the thickness of psoriatic plaque (Induration) and scaling (Scaling) are determined. These values are determined specifically for certain parts of the skin of the body: head, torso,

arms and legs and are finally added together. The PASI value ranges from 0, which indicates a disease-free state, to a maximum of 72. A PASI value above 10 indicates moderate to severe, and a PASI scores greater than 20 indicates severe psoriasis. Estimation of treatment effect was measured by PASI response relative to baseline PASI score. PASI-50 indicates a 50% reduction in the initial PASI score and indicates a mild improvement in skin lesions; PASI-75 indicates a 75% reduction in the PASI score which is interpreted as a marked improvement. PASI-90 means a 90% reduction in the initial PASI score and almost completely clean skin; PASI-100 signifies a 100% therapeutic response and complete withdrawal of skin lesions and completely clean skin (Silva et. al, 2013; Mattei et al., 2014; Oji & Luger, 2015).

Conventional treatments for moderate to severe psoriasis, including phototherapy with ultraviolet B (UVB), photochemotherapy with psoralens and ultraviolet A (PUVA), methotrexate, cyclosporine, and acitretin are limited by well-known and characteristic side effects, incomplete effectiveness in some patients, and demanding treatment schedules which result in decreased patient compliance (Bahner et al., 2009).

Fundamental research on the pathogenesis of psoriasis has substantially increased our understanding of skin immunology, which has helped to introduce innovative and highly effective therapies. (Grän et al., 2010). In the last two decades, a better understanding of psoriasis pathophysiology allowed the development of targeted therapies, including biologics, biosimilars and small molecules. Biologic drugs have revolutionized the treatment of psoriasis and other rheumatological diseases. Biologics and biosimilars are recommended as an option for moderate to severe plaque psoriasis as well as those with moderate to severe PsA (Gisondi et al., 2019; Kamata & Tada, 2020; Korman, 2020).

Since 2004, 11 biologics for psoriasis treatment have been approved by Food and Drug Administration (FDA) and the European Medicines Agency (EMA). These include etanercept, infliximab, adalimumab, ustekinumab, secukinumab, ixekizumab, guselkumab, tildrakizumab, risankizumab, and certolizumab pegol. According to the mechanism of action, biologics can be divided into several groups: antagonists of tumour necrosis factor-alpha (TNF-α), interleukin (IL) antagonists: (anti-IL-17A, anti-p40-IL12/23, anti-p19-IL 23, anti -p19/p40-IL 23) (Ivanić et al., 2021) (Table 1). All these biological medicines are given at defined intervals by subcutaneous injection or intravenous infusion.

Table 1. Mechanism of action, biological structure and biosimilars approved biological drugs for psoriasis

Biologics and mechanism of action	Biological structure
Anti-TNF-α	
Etanercept	Soluble TNFR2 coupled to the Fc portion of IgG1
Infliximab	Human/mouse chimeric IgG1mAb
Adalimumab	Human IgG1mAb
Certolizumab pegol	Humanized (from mouse) mAb, PEGYlated Fab fragment
Anti-IL-17A	
Secukinumab	Human IgG1 kmAb
Ixekizumab	Humanized IgG4 mAb
Brodalumab	Human IgG2 mAb
Anti-p40-IL12/23	
Ustekinumab	Human (IgG1)
Anti-p19-IL 23	
Guselkumab	Human IgG1 mAb
Tidrakizumab	Human IgG1λ mAb
Anti-p19/p40-IL 23	
Risankizumab	Humanized IgG1 aAb

TNF-α (tumor necrosis factor alfa); IgG (immuoglobulin G); IL (interleukin); mAb (monoclonal antibodies), p (portion); R (receptor)

Biosimilars are biotherapeutic products that are highly similar in terms of quality, efficacy and safety to an already licensed reference biotherapeutic product. Last nine years tumour necrosis factor (TNF)-alpha biosimilar agents have been approved for the treatment of psoriasis and other autoinflammatory conditions. Adalimumab, for convenience and efficacy reasons, is the most suitable for the treatment of psoriasis of the anti-TNFα agents with available biosimilars. Since 1913. the US FDA and /or the European Medicines Agency have approved eight biosimilars of adalimumab for the treatment of psoriasis. Given that these agents showed pharmacokinetic, efficacy, safety, and immunogenicity profiles comparable to those of the originator, adalimumab biosimilars were licensed for all indications approved for reference adalimumab based on extrapolation. (Puig et al., 2019; Reynolds et al., 2019; Zhou et al., 2021).

MATERIALS AND METHODS

Our research presents a retrospective cross-sectional study of the treatment effects on patients with moderate to severe plaque psoriasis with biologics and biosimilar drugs. These patients are currently being treated at the Clinic for Skin and Venereal Diseases of the University Clinical Center of the Republic of Srpska in Banja Luka.

The treatment of psoriasis with biological drugs in our Clinic started in June 2020. University Clinical Centre of the Republic of Srpska is the first institution in Bosnia and Herzegovina with biologics for psoriasis treatment. Biological drugs that we treat our patients with psoriasis are adalimumab (brand name Humira), adalimumab biosimilar (brand name Amgevita) and secukinumab (brand name Cosentix). Since these drugs are extremely expensive, patients are included in the therapy successively, depending on the approval by the Health Insurance Fund of the Republic of Srpska.

Adalimumab and adalimumab biosimilar are administered subcutaneously at a dose of 80 mg during the first week, 40 mg a week later, and then 40 mg every two weeks. Secukinumab is used in a subcutaneous dose of 300 mg once a week during the first 4 weeks, and then the treatment continues at 300 mg once a month.

Until this time this type of therapy is used by a total of 23 adult patients of both genders. PASI score was used to assess disease severity. Patients who had a PASI score ≥10–19 before treatment were rated as moderate psoriasis, and with a PASI score ≥ 20 as severe psoriasis. Out of the total number of respondents, 13 patients have been treated for more than a year, so we have results for them even after one year of treatment.

The effect of treatment of study patients was analyzed according to age, sex, duration of psoriasis and association with psoriatic arthritis (PsA). We evaluated the effects of biological and biologically similar drugs using PASI responses (PASI-50, PASI-75, PASI-90 and PASI-100).

Statistical analysis was performed using the SPSS 20 software package. The results were described descriptively, by mean values ($\bar{X}$), standard deviations (SD) for continuous variables, and percentages (%) for categorical variables. Differences between the mean values of the variables were analyzed using the independent samples t-test, while the differences between the frequencies of individual groups of patients were tested using the Chi-squared test. P values <0.05 are considered statistically significant.

RESULTS

Out of the total number of subjects in the study, only one patient due to psoriatic arthritis had previously been on biological therapy. Other patients are receiving biologics for the first time. Slightly more than half of the subjects (52.2%) receive biologics adalimumab (brand name Humira), 30.4% biosimilar adalimumab (brand name Amgevita), and the least secukinumab (brand Cosentix) (17.4%).

Almost two thirds (73.9%) of the respondents are male, while 26.1% are female. The result of the $\chi 2$ test shows that there is a statistically significant difference between the number of male and female patients ($\chi 2$ (2) = 5.261, p = 0.022).

At the start of biological therapy, the youngest patient was 19, and the oldest was 72 old. The mean age of patients was 40.87 ± 13.29 years, and 52.2% of patients were younger than 40 years. The results of the independent t-test indicate that there are no statistically significant differences in mean age between male and female patients (t (21) = -0.272, p = 0.788).

47.8% of patients with psoriasis are between 10 and 20 years old, 39.1% less than 10, and 13% of patients over 20. The results of the independent t-test indicate that there is no statistically significant difference in the duration of disease between male and female patients (t (21) = 0.196, p = 0.847). The results also show that in patients older than 40, the disease has lasted 22.6 years on average, which is 10.38 years longer than in patients younger than 40. This difference is statistically significant (p = 0.011).

Moderate plaque psoriasis is present in 52.2% of subjects, and severe psoriasis in 47.8%. The difference in the severity of the disease was not statistically significant (χ (1 = 0.15, p = 0.901).

In 31.1% of patients, psoriasis was associated with psoriatic arthritis, and 60.9% did not have affected joints. The difference is not statistically significant (p = 0.27).

Until now 39.1% of patients have been on biological therapy for more than one year, while in 60.9% of subjects the treatment lasts less than 12 months (Table 2).

Table 2. Demographic and clinical characteristics of the study group

Variables	Biologics			Total N%	P
	Adalimumab N%	Adalimumab biosimilar N%	Secukinumab N%		
Number of patients	12 (52.2)	7 (30.4)	4 (17.4)	23 (100.0)	
Age (years), $\bar{X}$ ± SD	45.50±13.43	31.86±11.77	42.75±8.77	40.87±13.29	0.788**
Age 18-39 years	5 (21.7)	6 (26.1)	1 (4.3)	12 (52.2)	
Age ≥ 40 years	7 (30.4)	1 (4.3)	3 (13.0)	11 (47.8)	
Gender					
Male	7 (30.4)	6 (26.1)	4 (17.4)	17 (73.9)	0.022*
Female	5 (21.7)	1 (4.3)	-	6 (26.1)	
Duration of psoriasis (years)					
< 10 years	6 (26.1)	3 (13.0)	-	9 (39.1)	
10-20 years	6 (26.1)	4 (17.4)	1 (4.3)	11 (47.8)	
>20 years	-	-	3 (13.0)	3 (13.0)	
Clinical type of psoriasis					
Moderate (PASI ≥10-19)	7 (30.4)	4 (17.4)	1 (4.3)	12 (52.2)	0.901*
Severe (PASI ≥ 20)	5 (21.7)	3 (13.0)	3 (13.0)	11 (47.8)	
Association with psoriatic arthritis					
Yes	5 (21.7)	3 (13.0)	1 (4.3)	9 (39.1)	0.279*
No	7 (30.4)	4 (17.4)	3 (13.0)	14 (60.9)	

*N (%) – number (percentage), $\bar{X}$ – mean, SD – standard deviation, PASI - Psoriasis Area and Severity Index, * Chi-squared test; ** independent t-test*

Until now 39.1% of patients have been on biological therapy for more than one year, while in 60.9% of subjects the treatment lasts less than 12 months.

Analysis of the PASI response after 16 weeks of biological and biosimilar treatment showed that most patients (60.9%) had a PASI-100 response, 17.4% PASI-90, and also 17.4% PASI-70. Only one patient (4.3%) had no improvement in biosimilar adalimumab therapy. The result of the $\chi 2$ test shows that there is a statistically significant difference ($p = 0.001$).

In 39.1% of patients on biologic therapy for more than a year, we assessed the PASI response after 12 months and found that half of the patients (50.1%) still had a PASI-100 response (completely clean skin), 21.5% PASI-90 (almost clean skin), and 7.1% PASI-70 (significant improvement in skin changes). Two patients experienced worsening psoriasis and their current biologic was replaced by another (Table 3).

Table 3. PASI response after 16 weeks and 12 months

Variables	Biologics			Total N%	P
	Adalimumab N%	Adalimumab biosimilar N%	Secukinumab N%		
PASI response after 16 week					
PASI-50	-	-	-	-	0.001*
PASI-70	2 (8.8)	1 (4.3)	1 (4.3)	4 (17.4)	
PASI -90	3 (13.1)	-	1 (4.3)	4 (17.4)	
PASI-100	7 (30.5)	5 (21.7)	2 (8.7)	14 (60.9)	
No improvement	-	1 (4.3)	-	1 (4.3)	
PASI response after 12 months	7 (30.4)	3 (13.0)	4 (17.4)	14 (39.1)	
PASI-50	-	-	-	-	0.143*
PASI-70	-	-	1 (7.1)	1 (7.1)	
PASI -90	3 (21.5)	-	-	3 (21.5)	
PASI -100	3 (21.5%)	2 (14.3%)	2 (14.3)	7 (50.1)	
Exacerbation	1 (7.1)	-	1 (7.1)	2 (14.2)	
Biological therapy replacement	-	1 (7.1)	1 (7.1)	2 (14.2)	

*N (%) – number (percentage); PASI - Psoriasis Area and Severity Index; * Chi-squared test;*

Due to the positive QuantiFERON test during treatment, biological therapy was temporarily excluded (for two months) in two patients, while in one female patient treated with adalimumab, therapy was completely excluded due to suspected demyelinating disease.

DISCUSSION

The results of our study are that all patients except one receive biological therapy for the first time and that two-thirds of the respondents are men. The number of patients with moderate to severe psoriasis and also those who have or do not have psoriatic arthritis at the same time is equal. By assessing the PASI response after 16 weeks, we found that most patients have a PASI-100 response and a PASI-90 which means clear or almost clear skin. We also found that one-half of patients who have received biologic therapy for more than one year, after 12 months maintain a PASI 100/90 response. Only two patients in the study who experienced worsening psoriasis biologics were replaced.

The efficacy of adalimumab in the treatment of psoriasis has been reported in numerous studies. Mijušković and the authors of their study state that adalimumab in psoriasis, leads to a PASI-75 response in 71% of patients after 16 weeks of therapy. According to another study, a PASI-75 response was achieved in 79%, and PASI-90 in 51.9% of patients. In the latter study, the efficiency was compared to methotrexate

in increasing doses (7.5 to 25 mg), which achieved PASI-75 in 35.5%, and PASI-90 in 13.6% of patients after 16 weeks of therapy. After therapy discontinuation, a rebound phenomenon was not reported, but continuous use is more efficient, taking into account the efficiency decrease after discontinuation and the reintroduction of adalimumab into therapy (Mijušković et. al, 2016).

In their research, authors state that at week 16, 71% of adalimumab and 7% of placebo-treated patients achieved greater than or equal to 75% improvement in the PASI score. During weeks 33 to 52, the percentage of patients rerandomized to placebo who lost adequate response (defined as < 50% improvement in the PASI response relative to baseline and at least a 6-point increase in PASI score from week 33) was 28% compared with 5% of patients treated continuously with adalimumab. Authors concluded that adalimumab is efficacious and well-tolerated in the treatment of chronic plaque psoriasis (Menter et. al, 2008).

The phase III randomized controlled evaluation of adalimumab every other week dosing in moderate to severe psoriasis trial (REVEAL) reported that the primary efficacy endpoint was the percentage of patients achieving at least 75% improvement in the PASI score at week 16. Post hoc subgroup analyses were conducted to determine relationships between adalimumab efficacy and/or safety and age group, sex, race, baseline weight intervals, baseline body mass index, disease duration, baseline severity, prior treatments, and comorbidities. that treatment of moderate to severe psoriasis with adalimumab led to consistent 75% or greater improvement in PASI score response rates across the majority of patient subgroups, with no significant differences in serious adverse events (Menter et. al, 2010). The conclusion of phase III clinical trial REVEAL in a 52-week trial of adalimumab therapy for moderate to severe chronic plaque psoriasis is that adalimumab efficacy was well maintained over more than 3 years of continuous therapy for patients with sustained initial PASI- 75 responses. Maintenance was best at the PASI-100 level (Gordon et al., 2012).

Adalimumab is well established for the treatment of moderate-severe chronic plaque psoriasis in adults and has been recently more approved by European Union for use in pediatric patients with severe chronic plaque psoriasis. (Wu & Valdecantos, 2017).

ABP 501, United States: AMJEVITA™ (adalimumab-atto); European Union: AMGEVITA® (adalimumab) is the first approved biosimilar to adalimumab (Markus et al., 2019; Constantin et al., 2019). Biosimilars are cheaper than original drugs and are thus of interest to the public (Barszczewska & Piechota, 2021; Zagni et al., 2021)

The efficacy of secukinumab in the treatment of psoriasis has been reported in numerous studies. Thus, Mijušković and the authors state that secukinumab is a recombinant, highly affinitive, completely human monoclonal IgG1κ antibody that binds selectively and neutralizes IL-17A. After 12 weeks, the recorded PASI-75 response in clinical studies was 81.6% and 77.1% (for 300 mg) and 71.6% and 67% (for 150 mg). Anti-secukinumab antibodies were detected in a very small percentage (0.3 to 0.4%) causing no reduction in therapy efficiency or occurrence of adverse effects. The most common adverse effects are nasopharyngitis, headaches and upper respiratory tract infections. In a study that compared the efficacy of secukinumab and ustekinumab, after 52 weeks, 76% of patients who were given secukinumab and 61% of the patients who were given ustekinumab had PASI-90, while 46% of patients who were given secukinumab and 36% of patients who were given ustekinumab achieved PASI-100 (Mijušković Ž. et al., 2016).

The results of the CLEAR study among 676 randomized subjects, also reported that secukinumab demonstrated sustained superior efficacy in comparison with ustekinumab in clearing skin through week 52, greater improvement in quality of life, and a favourable and comparable safety profile (Blauvelt et al., 2017).

In SCULPTURE extension study has been shown that secukinumab has significant efficacy and a favourable safety profile in the treatment of moderate-to-severe psoriasis and psoriatic arthritis. This study

was demonstrated rapid onset of response (50% of patients achieve PASI-75 at week 4 and sustainability of results over 5 years. PASI 75/90/100 response in year 1 (88.9%, 68.5% and 43.8%) was held over the next 5 years (88.5%, 66.4% and 41%). In the conclusion of this study, it is stated that secukinumab 300 mg treatment delivered high and sustained levels of skin clearance and improved quality of life over 5 years in patients with moderate-to-severe psoriasis. Favourable safety established in the secukinumab phase 2/3 programme was maintained for 5 years (Bissonnette et. al, 2018).

In the review, Berg et al. examine the efficacy and safety of secukinumab for the treatment of psoriasis using the literature retrieved from the PubMed database. In clinical trials, treatment with secukinumab led to rapid and sustained improvement in PASI scores, with PASI-90 response rates up to 68.5% at 5 years. Long-term clinical trials and real-world data have established secukinumab as a safe and effective treatment for psoriasis (Berg et. al, 2021).

Drug survival of biologics represents their real-world effectiveness and safety. In a multinational, prospective, observational study by Seneschal J, et al. the authors concluded that only one in four patients achieved complete skin clearance after 6 months of treatment with biologics (Seneschal et al., 2020). Also, it is none that the drug survival for all biologics decreased by a certain percentage with time. (Lin, 2018). However, it is very important for every patient with moderate or severe psoriasis if they have clean or almost clean skin for several years. This gives them hope for future cure for their disease.

CONCLUSION

The advancement of biologic therapy has made it possible to set new standards of efficacy and safety in the treatment of moderate to severe psoriasis. The results of numerous studies show that the use of biological therapy in the treatment of moderate to severe psoriasis has excellent results which can greatly prevent the development of significant comorbidities and contribute to improving the quality of life of these patients. Our study is limited by its small sample size, but confirms these results. With the development of biosimilar drugs whose price is about 30-40% lower than generic drugs, we can expect greater availability of modern therapy to a wider population of patients.

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Original scientific paper

The Effectiveness of Health Educational Materials in the Prevention of Non-Communicable Diseases

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ABSTRACT: Non-communicable diseases (NCDs) are the leading causes of morbidity, disability, and mortality among the world's population. In this research, we aim to determine the knowledge about the risk factors for NCDs, as well as socio-demographic differences in the effectiveness of health education materials in disease prevention. Instrument was prepared according to methodological guidelines for population health risks survey (Eurostat, 2018) and knowledge and attitudes related to NCD questionnaire survey. Sample size included 210 participants of both genders (N_{male}= 105, N_{female}= 105) systematically selected, residents of Belgrade, Republic of Serbia, who did not have diagnosed chronic non-communicable diseases and used services at primary health care centre Zvezdara. Research results indicate that 27% of all participants had one or more health educational activities in the last six months. More than two thirds of respondents (71%) know that tobacco usage is the leading cause of cardiovascular diseases, but 54,8% know that cause malignant diseases. More than two thirds of respondents know that inadequate nutritional habits, consumption of industrial products and sweets and low vegetable intake cause cardiovascular diseases and more than half of them know that inadequate nutritional habits causes malignant diseases. Statistically significance difference between groups of participants based on level of education are obtained in attitudes towards the effectiveness of health education material in the prevention of malignant diseases ($F= 3.396$, $p< .05$), diabetes ($F= 3.611$, $p< .05$) and respiratory diseases ($F= 3.483$, $p< .05$) and socio-economic differences in the use of printed and video materials in the prevention of NCDs. Effectiveness of health education materials through preventive activities improve health and reduce risks for NCDs.

Keywords: knowledge, attitudes, cardiovascular diseases, malignant diseases, risk factors.

INTRODUCTION

Despite the implementation of different programs in the field of public health and the implementation of interventions aimed at reducing risk factors (Jović, 2016), the leading problems in the 21st century on a global level are social consequences of urbanization and increased exposure to risk factors for non-communicable diseases (NCDs) (Ramić-Čatak, 2017). Chronic diseases are the leading causes of death and disability worldwide, and prevalence of those diseases is rising sharply, and progressing in all regions within all socio-economic classes. Main risk factors for chronic diseases are cigarette consumption, exposure to tobacco smoke, poor diet, lack of physical activity and excessive alcohol consumption (WHO, 2014a,b; CDC). According to data of population health in the Republic of Serbia, one-third of population over the age of 20 have hypertension (Stojadinović et al., 2014), while in addition to irregular physical activity and obesity, cardiovascular disease can occur as a consequence of osteoporosis in the elderly (Tasić et al., 2014). Leading risk factors for the development of cardiovascular and malignant diseases are tobacco and alcohol use, improper diet, and insufficient physical activity (Šiljak, 2019).

Due to significant percentage of countries face various forms of chronic diseases, the need for preventive activities in the community, families, organizations, regions, and different social strata has never been greater (Sranacharoenpong & Hanning, 2011; Bhattarai et al., 2019). Under the umbrella of organised health care preventive programmes, the incidence of risk factors for chronic diseases could be controlled

(Eminović, 2018). The health care system should be equipped to provide all necessary materials for information, education, and counselling for health promotion in health facilities (Parker et al., 2012). Media techniques, printed materials, advertising materials, computer methods, and printed media, such as posters, leaflets, magazines, and articles, are commonly used forms of information providing health and preventive health care (Vuković, 2012). Prevention programs and adequate health education of the population can improve overall well-being and reduce the rate of diseases to a minimum (Bonnie, Stroud & Breiner, 2014).

The usefulness of simple health education materials for education of population and evaluation of health promotion and prevention programs increases in the health care system. The design and implementation of effective health education materials is a systematic process, which begins with a definition of educational goals, production, participation of different profiled experts, and its validation (Arora et al., 2017). Environmental factors could have positive and negative impacts on health (Šiljak, 2019). The positive impact is oriented on provision of accessible primary and secondary education, health care, and general hygienic aspects related to housing, regardless of the social status of the individuals. The negative impact on health could be reflected on various risk factors from the place of living and working environment. Activities in area of health promotion and diseases prevention are focused on individual's behaviour in relation to social, cultural, and organizational factors, active participation in preventive activities in community, as well as the development and implementation of activities (Koelen, Vaandrager & Colomér, 2001).

Given the fact that an increasing number of residents are at risk for various chronic diseases, this paper aims to determine the knowledge and attitudes to the risk factors for NCDs, as well as effectiveness of health education materials in the disease prevention based on socio-economic status and level of education of participants.

MATERIAL AND METHOD

The research was conducted in Belgrade, at Zvezdara Health Center, which is located in municipalities of Vračar, Voždovac, and Novi Beograd, during spring 2021. Sample size included 210 participants older than 18 years, of both genders (N_{male}= 105, N_{female}= 105) systematically selected, residents in Belgrade, Republic of Serbia, who don't have diagnosis of chronic diseases, giving the consent in participation of study, and using services at primary health care centre Zvezdara.

For the purposes of this research instrument was prepared according to standard methodological guidelines for population health risks survey (Eurostat, 2018) and questionnaires about knowledge and attitudes related to NCD from similar scientific and professional manuscript. Participation in research was anonymous. Questionnaire was prepared in three parts. The first part was used for collecting basic sociodemographic characteristics of participants (gender, age, level of education, socio-economic status, etc.). Gender is classified as male and female, while age groups are classified in ten groups of respondents older than 18. Level of education is classified as primary, secondary and high level of education, while socioeconomic status categorized as poor, average and good. The second part of questionnaire provides insight into the exposure of respondents to risk factors (smoking, alcohol, physical activity, and nutritional habits), knowledge, and views about their impact on the occurrence of NCDs (cardiovascular diseases, cancer, diabetes, respiratory diseases). The level of knowledge and attitudes was assessed on a three-point scale with accuracy of statement on risk factors related to NCD (yes, no, and not sure). The last part was intended to collect attitudes of respondents regarding the importance and impact of health educational material in NCDs prevention. The level of agreement with the statements, from the strongest to the weakest level of agreement, was determined by a five-point Likert-type scale. A higher score, obtained on the basis of the respondents' answers, indicates a higher result and a more positive attitude of the respondents towards the stated statement. The Ethics Committee of the Primary Health Centre approved the study.

Descriptive statistical methods were used to describe the data. To assess the significance of the difference in individual attitudes of respondents based on socio economic status and level of education were determined by One-way ANOVA, while the post-hoc Tukey test was used to confirm the differences occurred between groups. For all applied analytical methods, statistically significant was the value of error probability $p < 0.05$. The statistical package for social sciences was used in data processing (SPSS for Windows, version 21.0, 2012).

RESULTS

Out of 210 participants (N_{male} = 105, Nf_{emale} = 105) included in the study 12.4% were in age groups (31–35 years and 36–40) years old, respectively. According to the level of education, most of respondents (52.8%) have high school, 75,7% are employed, with mainly monthly income between 10 001-30 000 RSD (85 EURO) and living in average social status (48,1%) (Table 1). Only 27% of participants had the experience of participation in preventive services in the last six months.

Table 1. Demographic and socio-economics characteristics of participants (N=210)

	Total	
	N	**%**
Gender		
Male	105	50
Female	105	50
Age group		
18-24	19	9
25-30	16	7.6
31-35	26	12.4
36-40	26	12.4
41-45	20	9.5
46-50	17	8.1
51-55	22	10.5
56-60	15	7.6
61-65	25	11.9
+ 65	23	11
Education level		
Primary	5	2.4
Secondary	94	44.8
High school and Faculty	111	52.8
Employment status		
Unemployed	9	4.3
Employed	159	75.7
Other (pensioner, student, other)	42	20
Socio-economic status		
Poor	39	18.6
Average	101	48.1
Good	70	33.3
Monthly level of income per family member		
under 10 000 RSD (under 85 EURO)	2	1
10 001- 30 000 RSD (86-254 EURO)	97	46.2
30 001- 50 000 RSD (255-424 EURO)	51	24.3
+ 50 000 RSD (+425 EURO)	60	28.6
Experience in participation in preventive activities		
Yes	56	27
No	154	73

The knowledge about the risk factors for NCDs (Table 2), examined through this research, have shown that the usage of tobacco products is leading risk factor for cardiovascular (71%) and malignant (54.8%) diseases based on the answers. The usage of alcoholic products is the risk factor for cardiovascular diseases, by the answer of 94 (44.8%) respondents, while the same percentage was not sure that these products are the risk factors for their occurrence. About half of the respondents (46.7%) were unsure that alcoholic products could initiate development of malignant diseases. In most cases of answers, physical inactivity was one of the risk factors for cardiovascular diseases (43.3%), but not for malignant diseases (56.7%). A high percentage of participants shared the thought that consumption of industrial products, sweet beverages, and cakes and insufficient consumption of vegetables were the risk factors for cardiovascular (77.1%:84.8%) and malignant diseases (44.3%:56.7%). More than 40% of respondents are not sure that alcohol and physical inactivity are risk factors for cardiovascular diseases, and each fifth respondents is not sure that industrial products and sweet beverages lead to cardiovascular diseases (Table 2).

Table 2. Knowledge and attitudes to the risk factors for NCDs

Risk factors	Cardiovascular disease						Malignant diseases					
	Yes		No		Not sure		Yes		No		Not sure	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Tobacco products use	149	71	20	9.5	41	19.5	115	54.8	17	37.1	78	37.1
Alcohol products use	94	44.8	22	10.5	94	44.8	69	32.9	43	20.5	98	46.7
Physical inactivity	91	43.3	27	12.9	92	43.8	58	27.6	119	56.7	33	15.7
Consumption of industrial products, sweet beverages and cakes	162	77.1	5	2.4	43	20.5	93	44.3	14	6.7	109	49
Insufficient consumption of vegetables	178	84.8	7	3.3	25	11.9	119	56.7	31	14.8	60	28.5

Table 3 shows the differences in attitudes towards the effectiveness of health education materials in NCDs prevention based on level of education and socio economic status of participants. Statistically significance difference between groups was obtained in attitudes towards the effectiveness of health education material in the prevention of malignant diseases ($F= 3.396$, $p<0.05$), diabetes ($F= 3.611$, $p< 0.05$) and respiratory diseases ($F= 3.483$, $p< 0.03$). Respondents with primary level of education found that health education material is important in the prevention of malignant diseases, while those with high level of education found it more important in prevention of diabetes and respiratory diseases. Respondents who are living in poor socio-economic conditions have strongly agreed on the impact of printed ($F= 5.817$, $p= 0.01$) and video health education material ($F= 4.945$, $p= 0.01$) in the prevention of NCDs.

Table 3. Attitudes towards the importance of health education material in the disease prevention

Attitude Health education material is important	Level of education	M	SD	F	p	Socio economic status	M	SD	F	p
In the prevention of malignant diseases	High	3.68	1.09	3.396	0.03	Good	3.70	0.98	1.53	0.21
	Secondary	3.32	1.07			Average	3.43	1.00		
	Primary	3.80	0.99			Poor	3.46	1.21		
In the prevention of diabetes	High	3.76	1.30	3.611	0.02	Good	3.81	0.94	2.894	0.06
	Secondary	3.39	1.06			Average	3.44	0.99		
	Primary	3.20	0.96			Poor	3.54	1.21		

In the prevention of cardiovascular diseases	High	3.95	1.22	1.505	0.22	Good	3.80	1.00	1.314	0.27
	Secondary	3.70	1.13			Average	3.77	1.02		
	Primary	4.00	0.91			Poor	4.08	1.08		
In the prevention of respiratory diseases	High	3.55	1.58	3.483	0.03	Good	3.49	0.93	0.592	0.55
	Secondary	3.20	1.07			Average	3.32	0.95		
	Primary	3.00	0.89			Poor	3.36	1.27		
In the prevention of hypertension	High	3.69	1.14	1.490	0.23	Good	3.80	0.88	2.846	0.06
	Secondary	3.47	1.04			Average	3.45	0.91		
	Primary	3.40	0.88			Poor	3.56	1.19		
For prevention of disability, as a consequence of various condition and diseases	High	3.75	1.30	2.068	0.13	Good	3.79	0.95	1.629	0.19
	Secondary	3.47	1.05			Average	3.50	0.95		
	Primary	3.80	0.94			Poor	3.64	1.20		
Used in printed form in the prevention of non-communicable diseases	High	3.37	1.14	0.692	0.50	Good	3.51	1.06	5.817	0.01
	Secondary	3.23	0.98			Average	3.08	0.78		
	Primary	3.60	0.99			Poor	3.56	1.19		
Used as a video material in the prevention of non-communicable diseases	High	3.42	1.18	0.130	0.88	Good	3.60	1.18	4.945	0.01
	Secondary	3.37	1.05			Average	3.15	1.02		
	Primary	3.20	1.30			Poor	3.67	1.13		

M- mean, F- ANOVA F statistic value, p- Statistical significance level

The content of health education material has an important role in change of risk behaviour and improvement of own health. Based on data shown in Table 4, it was obtained that content of the health education material improves knowledge and change behavior toward own health mainly by respondents with high level of education and living in good socio economic status without significance differences between groups of them. Furthermore, respondents with better life conditions based on good socio-economic status and high level of education have increased awareness of the importance of health educational material focused on prevention and motivation to improve own health.

Table 4. Attitudes towards the effectiveness of the content of health education material in the disease prevention

Attitude **Content of health education material**	**Level of education**	**M**	**SD**	**F**	**p**	**Socio economic status**	**M**	**SD**	**F**	**p**
Improves knowledge and change behavior toward own health	High	3.77	0.94	1.869	0.16	Good	3.86	1.04	2.649	0.07
	Secondary	3.51	1.08			Average	3.50	0.97		
	Primary	3.40	1.34			Poor	3.67	1.08		
Improves knowledge and changes the behavior towards the health of others in the community	High	3.72	1.34	2.835	0.06	Good	3.70	1.04	0.970	0.38
	Secondary	3.39	1.06			Average	3.49	0.86		
	Primary	3.40	0.91			Poor	3.54	1.25		
Stimulates a healthy lifestyle	High	3.95	1.14	2.643	0.07	Good	3.94	0.95	0.967	0.38
	Secondary	3.66	1.02			Average	3.75	0.91		
	Primary	3.60	0.85			Poor	3.74	1.04		
Increases motivation to improve health	High	3.95	1.34	2.516	0.08	Good	4.00	0.96	2.051	0.13
	Secondary	3.68	0.99			Average	3.71	0.88		
	Primary	3.40	0.87			Poor	3.74	1.07		
Increases the degree of responsibility for own health	High	3.76	1.30	0.847	0.43	Good	3.77	1.02	0.838	0.43
	Secondary	3.67	1.03			Average	3.61	0.95		
	Primary	3.20	0.95			Poor	3.82	1.07		
Increases awareness of the importance of prevention	High	3.69	1.14	0.601	0.54	Good	3.76	1.03	1.624	0.20
	Secondary	3.56	0.99			Average	3.50	0.86		
	Primary	3.40	0.94			Poor	3.72	1.09		

Provides adequate guidelines for the use of preventive health services	High	3.76	1.58	1.933	0.14	Good	3.73	0.90	0.307	0.74
	Secondary	3.62	0.95			Average	3.62	0.88		
	Primary	3.00	0.87			Poor	3.72	1.12		
Provides new information on prevention activities	High	3.80	1.30	2.398	0.09	Good	3.81	0.92	1.110	0.33
	Secondary	3.56	0.97			Average	3.60	0.83		
	Primary	3.20	0.86			Poor	3.64	1.16		
Provides insight into risk factors and ways to overcome them	High	3.75	1.51	0.414	0.66	Good	3.74	1.03	0.176	0.84
	Secondary	3.63	0.94			Average	3.65	0.91		
	Primary	3.60	0.96			Poor	3.69	1.00		

M- mean, F- ANOVA F statistic value, p- Statistical significance

DISCUSSION

Health education and preventive services implemented through promotional and preventive activities aims to ensure the elementary health needs of the population (Šiljak, Niškanović & Stojisavljević, 2018). Preventive activities in area of health education using of health promotional materials and implementation of continual preventive activities are considerable in the education of society about potential risk factors and actions to prevent the occurrence of NCDs. According to the data of the Institute of Public Health of Serbia, "Dr. Milan Jovanović Batut'', programmes of health education in Belgrade primary health care centres, during 2018, were realized by applying various health education methods (Miltenović, 2020). Preventive health activities on the territory of the city of Belgrade were realized both in health centres and in the community by health professionals and associates. Of 210 participants, in total, 154 (73%) did not have experience related to the health education and health education material in the last six months, which is lower than in European and Asian Counties (Amaraskera, 2016;Tedesco, 2014).

Factors such the use of processed foods, rapid urbanization, lifestyle changes and changes in eating habits characterized by excessive intake of salt, sugar and usage of tobacco products resulting in a drastic increase in cardiovascular diseases such as hypertension, heart attack, and others (Rajnarayan et al., 2006; Šarčević, Lilić & Vranić, 2014; Tasić et al., 2014; Mikkelsen et al., 2019;). Studies from the South-East Asian region, Eastern Mediterranean, and European region show that smoking cause oral and oesophageal cancers, pancreatic cancer, stomach, kidney, liver, bladder, cervix, colon, and rectum, as well as leukemia, and high risk of death from lung, cervical and prostate cancer (Wang et al., 2017; Gupta et al., 2018; Božić et al., 2020). Therefore, it is important to underline that specifically adequate knowledge, positive attitudes and health promotion behaviours regarding to CVD could reduce incidence of the diseases. The level of knowledge about risk factors (smoking, alcohol consumption and inadequate nutritional habits) regarding CVD by more than half of respondents was adequate which is similar to studies in Italy (Tedesco, 2014), India (Poudel, 2017) and Iran (Mazloomy,2013). The majority of respondents, more than two thirds of them, know that inadequate nutritional habits (consumption of industrial products, sweet beverages, and cakes and insufficient consumption of vegetables) are the risk factors for cardiovascular and malignant diseases. In Italian study more than 60% of people know that high salt diet cause CVD (Tedesco, 2014), while in French study highest risks for CVD are fat diet, smoking and physical inactivity (Kelly-Irving, 2010). In the United States study among young adults' knowledge of CVD risks factors are most corrected for smoking, saturated fat found in animal products and high blood cholesterol (Winham, 2011).

Research data showed that insufficient physical activity is directly related to mortality and morbidity of NCDs (Jakovljević & Đorđević, 2017; Ding, 2018; Medina et al., 2021).

According to our study results, physical inactivity is risk factor for cardiovascular disease for more than 40% of respondents, in Italian study 47,3% of people (Tedesco, 2014), which is similar to study in

New England (Gans, 1999) in which highest knowledge score for CVD were physical inactivity and high fat diet. One of the segments of this research was to determine the attitudes towards the effectiveness of health education materials in NCDs prevention. Results of our research show that the content of health education material can be important for motivation and improvement of health and lifestyle related to health behaviour. Significant differences based on participants' socio-economic status and level of education were obtained. Namely, participants with good socio-economic status and high level of education had positive attitudes towards importance of health education material in motivation and improvement of healthy lifestyle than other groups of participants, which is similar to studies in India (Verma, 2019), Sri Lanka (Amarasekara, 2016) and Iran (Koohi, 2020). Also, participants with good socio-economic status and high level of education had positive attitudes towards the importance of health education material in malignant diseases and diabetes mellitus prevention. The results on the effects of preventive activities and the health education methods used correspond to similar research in Europe and Asia (Baker, 2011; Parker, 2012; Mikkelsen, 2019, Wu et al. 2017; Winham, 2011). Low level of education of respondents was associated with usefulness of printed health education materials as well as in study in England (Maskell, 2018) and Kentucky, United States (Ryen, 2014).

The health care system's functioning, planning, and implementation of preventive activities can be improved by continuous and relevant data collection within all health care levels. There is a small number of researches aimed to assess the effectiveness of health education materials and methods in NCDs prevention in Republic of Serbia. The importance of the conducted study reflects the acquisition of preliminary insight into the following: individuals' knowledge of main risk factors for NCDs and the attitudes towards using health education materials in preventive activities. The limitations of our study are relatively small sample size in one municipality in Belgrade and a survey provided only with beneficiaries of health care services.

CONCLUSION

Non-communicable diseases can occur under the influence of different risk factors. According to the research results, more than half of respondents knows that tobacco products and insufficient consumption of vegetables cause cardiovascular and malignant diseases. More than one third of respondents knows that alcohol and physical inactivity cause cardiovascular diseases. Approximately half of them are not sure that alcohol products and consumption of industrial products or sweet beverages cause malignant diseases.

There are socio-demographic differences in attitudes towards the effectiveness of health education material. Usefulness of printed and video health education material is strongly confirmed by respondents living in poorer socio-economic conditions while those highly educated strongly agree about the usefulness of health educational material in the prevention of diabetes and respiratory diseases. Respondents living in better life conditions have positive attitudes towards using health educational material for the improvement of own health.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Original scientific paper

The Incidence of Contrast Induced Nephropathy in Major Trauma Patients in the University Clinical Center of the Republic of Srpska

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ABSTRACT: Contrast-induced nephropathy (CIN) is characterized as an acute renal injury after the administration of intravascular iodinated radio-contrast medium in the absence of any other etiology. There is a small number of studies that analyze the occurrence and impact of CIN in traumatized patients who require whole-body CT according to the polytrauma protocol. In the period from January 2021 to May 2022, patients in the University Clinical Center of the Republic of Srpska who underwent CT according to the protocol for polytrauma were retrospectively analyzed. The study included 51 patients. CIN was defined as a 25% rise from baseline creatinine, or an absolute increase in creatinine of ≥ 44 μmol/l 24–48 h after administration of contrast. Of the total number of patients, 12% (n = 6) met the criteria for CIN. Age, sex, comorbidity, severity of injury based on ISS (injury severity score) were analyzed. Hemoglobin and fibrinogen levels, length of hospitalization, stay in the intensive care unit, mortality were monitored. A value of $p < 0.01$ was considered statistically significant. CIN is common in traumatized patients, but it is not an independent risk factor for length of hospitalization or mortality.

Keywords: Contrast Induced Nephropathy, Trauma, Computed Tomography.

INTRODUCTION

The intravascular administration of iodinated radiocontrast media can lead to acute renal dysfunction, which in the absence of other causes is defined as contrast-induced nephropathy (Weisbord & Palevsky, 2005).

The proposed pathophysiologic mechanisms of CIN are complex including intrarenal vasoconstriction with resultant medullary hypoxia, generation of reactive oxygen species, and direct renal tubular toxicity.

The pathophysiological mechanism of contrast-mediated nephropathy (CIN) is not completely clear. It is most likely due to vasoconstriction of intrarenal blood vessels with consequent medullary hypoxia, release of oxidative factors and direct renal tubular toxicity (Hossain et al., 2018).

It is a reversible impairment of renal function with an increase creatinine levels at 2-3 days and returning to baseline within 7-10 days after the administration of contrast medium.

There is no specific therapy for CIN, so risk assessment and the implementation of certain prophylactic measures are extremely important to reduce morbidity and mortality. CIN risk assessment is performed based on eGFRs (estimated glomerular filtration rates). Patients with eGFRs ≥ 45mL/min/1.73m2 have a minimal risk of CIN, patients with eGFRs < 30mL/min/1.73m2 are at high risk of CIN, while patients with eGFRs between 30 and 44mL/min/1.73m2 have a medium risk of development of CIN which is particularly increasing in diabetic patient (Rudnick et al., 2020; Tao et al., 2016). CIN is commonly diagnosed as an increase in creatinine value of 25% compared to normal values or an increase in initial creatinine value by ≥ 44 μmol/l 24–48 h after iodine contrast agent administration (Feldkamp & Kribben, 2008).

The incidence of CIN varies from 0.6 to 2.3% in patients who have not previously had impaired renal function, while in patients with increased risk factors it is up to 30% (Feldkamp & Kribben, 2008). Older age, diabetes, previous kidney disease, volume depletion, heart failure, and the use of nephrotoxic drugs are risk factors for developing CIN (McCullough, Wolyn, Rocher, Levin, & O'Neill, 1997; Owen, Hiremath, Myers, Fraser-Hill, & Barrett, 2014).

Contrast enhanced whole-body CT is more and more routinely performed for the initial evaluation of severely injured patients (Gordic et al., 2015). Although there is an increased risk, there are few studies that analyze the incidence and clinical significance of CIN in polytraumatized patients (Kelemen et al., 2022).

MATERIAL AND METHODS

This is a retrospective research, for the implementation consent of the Ethics Committee of the University Clinical Centre of the Republic of Srpska was obtained. Patients with a referral diagnosis of polytrauma, admitted to the Emergency Department of the University Clinical Centre of the Republic of Srpska between January 2021 and May 2022, were retrospectively analyzed. The study included patients older than 18 years who had CT performed according to the polytrauma protocol immediately upon admission. The study did not include patients who died in the first 24 hours after admission and patients who did not have recurrent creatinine levels 24 and 48 hours after iodine contrast agent administration. Patients with repeated CT diagnostics with contrast in the first 48 h were also excluded from the study. The study included a total of 51 (n = 51) patients.

CT according to the protocol for polytrauma in University Clinical Centre of the Republic of Srpska means native CT of the head and neck followed by contrast application of 1 ml/kg TT of isosmolar, non-ionized contrast containing 300 mg of iodide per milliliter (Ultravist®; Bayer Healthcare, Leverkusen, Germany) with saline lavage at a dose of 30 ml for chest and abdominal imaging.

Patients selected according protocols from the Emergency Department of the University Clinical Centre of the Republic of Srpska in the mentioned period, and the data were obtained from the clinical information system. Demographic data were collected: age, sex, comorbidity, severity of injury based on ISS (Injury Severity Score) (Elgin, Appel, Grisham, & Dunlap, 2019), length of hospitalization, hospitalization in the intensive care unit and mortality. The values of hemoglobin and fibrinogen (g/L) at admission, creatinine level at admission, creatinine level 24 and 48 h after CT imaging according to the polytrauma protocol were monitored. The need for transfusions of blood derivatives in the first 24 hours after admission was analyzed. The aim of this study was to analyze the incidence of CIN in polytraumatized patients, to identify risk factors for CIN in this group of patients, and to indicate the impact of CIN on treatment outcome. CIN was defined as a 25% increase in creatinine from normal or an increase in baseline creatinine of ≥ 44 μmol/l 24–48 h after iodine contrast agent administration (Feldkamp & Kribben, 2008).

The incidence of CIN in polytraumatized patients was expressed at 95% confidant interval (CI).

Categorical data are presented as frequency and numerically as mean ± standard deviation (SD). The Chi - square test was used to compare categorical variables and the Mann–Whitney U-test for numerical data.

All statistical analyses were performed by IBM SPSS. A p value of <0.01 was considered statistically significant.

RESULTS AND DISCUSSION

There are a small number of studies on the occurrence of CIN in major trauma patients. Most of the research about CIN have been performed in patients undergoing percutaneous coronary interventions (PCI) (McCullough et al., 1997). Cause of creatinine increase in severely injured patients can be multifactorial e.g., hemorrhagic shock, blood transfusions, injury mechanism, rhabdomyolysis advanced age (Kelemen et al., 2022).

Our study included a sample of 51 patients. Of the total number of patients, 6 or 12% met the criteria for CIN. Table 1 shows the differences between patients with CIN and those who did not develop renal impairment 8 (non-CIN) in terms of age, sex, comorbidity, ISS, hemoglobin and fibrinogen levels, need for transfusion, length of hospital stay (LOS) and length of stay in the intensive care unit (ICU).

In a retrospective cohort study conducted in Zurich, 14% of patients had CIN (Kelemen et al., 2022). This study was conducted over a long period of time, included 284 patients, was performed in the trauma center of the first degree and referred to polytraumatized patients who were intubated at admission and with a significantly high ISS. Other similar studies showed a significantly lower prevalence of 2.1 to 5.1% (Colling et al., 2014).

Our study included 8 (15.68%) women and 43 (84.32%) men. All patients who had CIN were male, but due to the small number of patients who had CIN, the influence of gender on the occurrence of CIN cannot be proven.

The age analysis showed that the mean value of years in the CIN group was 49 ± 18 and in the second group it was 48 ± 19 ($p = 0.0001$). Age is considered to be a significant risk factor for CIN (Colling et al., 2014) , which has been confirmed in our study.

A significant factor for the development of CIN is comorbidity. This has been proven by results of similar studies (Toprak et al., 2007). We analyzed the presence of cardiovascular disease, diabetes mellitus and previous kidney disease. However, possibly due to the small sample group of our study and the large variety of preexisting conditions, we haven not proven that the presence of comorbidities significantly influenced the occurrence of CIN ($p = 0.8471$).

The ISS (Injury Severity Score) has been used to estimate the severity of trauma since 1974, the value can be from 0-75. The ISS score in our patients in the CIN group was 22 ± 11, and in the non-CIN group 14 ± 7. We have not ben able to prove a significant statistical difference between these two groups ($p = 0.4718$). In a retrospective cohort study (Kelemen et al., 2022) in the CIN group the ISS was 30 ± 16 and in the non-CIN group 28 ± 17 ($p = 0.296$). In this study, patients admitted to the trauma center was endotracheal intubated. Our study included patients who had a referral diagnosis of polytrauma, while data on how many patients were intubated prior to hospitalization were not available.

The mean hemoglobin level (g/L) in the CIN group was 12.9 ± 1.7. In the non-CIN group it was 13.6 ± 1.8 ($p = 0.001$). The value of fibrinogen (g/L) in the CIN group was 2.7 ± 0.9 and in non-CIN 2.6 ± 0.5 ($p = 0.4443$). Low hemoglobin levels at admission have been reported as a risk factor for nephropathy in patients undergoing coronary angioplasty (Spahn, Spahn, & Stein, 2015). In major trauma patients, anemia was not assessed as a significant risk factor for CIN, but CIN in combination with low hemoglobin levels doubled the mortality in their population (Banda et al., 2016).

In our study, 67% of patients in the CIN group and 40% of patients in the non-CIN group required a transfusion in the first 24 hours. Erythrocyte transfusion is a significant risk factor for renal impairment, studies have shown that each unit of erythrocyte increases the risk of nephropathy by 10 to 20% in cardiac surgery patients (Karkouti, 2012).

No patient in our study required hemodialysis in the first 48 h after trauma. Similar studies have not shown that CIN significantly increases the risk of hemodialysis in trauma patients (McDonald et al., 2014).

The mean length of hospital stay in the CIN group was 16.8 ± 9.6 days, while in the non-CIN group it was 11,4 ± 10,7 days. Possibly due to the large variety in length of stay in both groups, we have not been able to prove a significant statistical difference between these two groups (p = 0.4408) which showed that in our study the occurrence of CIN did not certainly affect the length of hospital stay. The mean number of hospitalization days in the intensive care unit (ICU) in the CIN group was 7 ± 7 days and in the non-CIN group 5 ± 8 days. All patients in our CIN group stayed in intensive care for at least 1 and at most 19 days. Not all patients in our non-CIN group stayed in intensive care. That might indicate that patients in CIN group dealt with more serious injuries than those in non-CIN group, but for making any further correlation larger sample group is needed.

No patient died in CIN group in our study. Furthermore, in the study (Kelemen et al., 2022), CIN did not affect mortality and duration of treatment.

There are some limitations to this study. This study was conducted on a small sample, conducted retrospectively in a short period of time. The study included patients who underwent contrast-enhanced CT according to the polytrauma protocol. There are no clearly defined criteria for whole body CT for major trauma patients. Medical records are often incomplete, a large number of patients could not be included due to lack of individual data. Lactate levels were not analyzed, as a factor that would indicate hypovolemia and the presence of shock. No data were available on the amount and application of crystalloid solution in the first 24 or 48 hours after trauma.

Table 1. Summary of patient characteristics between the CIN and non-CIN group

	Non-CIN n = 45 (88%)	CIN n = 6 (12%)	p value
Age (years)	48 ± 19	49 ± 18	0.0001
Gender (male)	37 (82%)	6 (100%)	0.5628
Comorbidities	12 (27%)	4 (67%)	0.8471
Injury severity score	14 ± 7	22 ± 11	0.4718
Hemoglobin (g/l)	13.6 ± 1.8	12.9 ± 1.7	0.0001
Fibrinogen	2.6 ± 0.5	2.7 ± 0.9	0.4453
Transfusion	18 (40%)	4 (67%)	0.7805
Length of stay (days)	11,4 ± 10,7	16.8 ± 9.6	0.4408
Stay in the intensive care unit (days)	5 ± 8	7 ± 7	0.3652

CONCLUSION

Based on the obtained data, we have concluded that the use of iodine contrast agent in the diagnostic treatment of major trauma patients does not lead to additional damage in these patients. The development of CIN does not certainly lead to prolonged hospitalization or increased mortality. Polytraumatized patients, especially those with high ISS, require contrast-enhanced CT, regardless of the risk of CIN. There are other risk factors for kidney damage in these patients. Additional research is needed to examine the effect of fluid and blood transfusion, the mechanism of injury, the injured part of the body on the development, as well as the consequences of CIN in these patients.

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Original scientific paper

Analysis of Microbiological Tests in Urinary System Infections

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ABSTRACT: Urinary tract infections account for about 40% of overall hospital system infections and are a serious economic burden and problem for public health system in any country. This is primarily expressed through absence from work. Urinary infection analysis needs to provide better results in this field by improved and better quality prevention, better education, and also higher quality hospitalisation. Using the method of urine analysis, i.e. through its results, we come to understand what the most common causes of urinary infections are. The study shows that the bladder inflammation (N30) is the most common admitting diagnosis in subjects whose urine culture was positive. Among the subjects with positive urine culture, Escherichia coli was found in 43.4% of patients. A statistically significant association was found between admitting diagnoses and the age group of respondents aged 35 to 50.

Keywords: Urinary tract infection, urine culture, Escherichia coli, immunity.

INTRODUCTION

The urinary system (lat. Organa urinaria) (US) is a group of human organs that have a task and role in:

- regulating the volume and composition of bodily fluids
- elimination of excess water, electrolytes and toxic substances (urea and creatinine) from the body
- cleansing the blood plasma of unwanted substances.

With the entry of pathogenic microorganisms into the human body, a biological process occurs which we call infection or contagion. Infection in most cases is caused by microorganisms after their entering the human body, and the most common are: bacteria, viruses, fungi and parasites. Since the human body neutralizes microorganisms with its immune system, every infectious process does not turn into a disease.

The most important factors for the development of infections are: the way microorganisms enter the body, the number of microorganisms and their power.

The most common infection, which occurs three or more times a year, and which occurs more often in women than in men, is urinary system infection (USI).

The main cause of cystitis and pyelonephritis is Escherichia coli. It is a type of bacteria that lives in the intestines of the human body, and under normal conditions does not lead to infections. It causes infection by creating various symptoms (discomfort and pain). Among other bacteria that also cause urinary tract infections, we note: proteus mirabilis, klebsiella, streptococcus agalactie, pseudomonas aeruginosa, enterococcus faecalis.

By the method of urine analysis, we find out what the state of a person's metabolism is, as well as the state of their urinary system. In addition to being a basic laboratory analysis, urine examination is an important diagnostic method.

The aim of the research was to determine the frequency of individual causes of urinary system infections, and to examine the interrelationships of respondents' demographic characteristics, as well as the relations between family physicians' admitting diagnoses and the results of laboratory analysis.

MATERIALS AND METHODS

The study included women of reproductive age from 18 to 50 from the Posavina County, who, in the period from January 1, 2021 to June 30, 2021, due to suspected urinary system infections, were referred to the Institute for Public Health Care for microbiological analysis by family doctors. The data indicated on each referral to the laboratory were used in this research, namely: age, place of residence and admitting diagnosis.

In the Public Health Institute of the Posavska County in Orašje, a microbiological examination of 249 urine samples taken from women from the Posavska County with suspected urinary system infection was performed.

Urine was processed according to the regulations related to microbiological analysis in such a way that the urine passed an automatic device that works on the principle of incubation of urine and has a reader of positive cultures.

Isolation of all urine cultures that were positive in the device and that contained more than or equal to 104 CFU/ml of microorganisms was performed. Positive urine samples were inoculated on CPSE nutrient medium at 37 degrees Celsius for about 24 hours.

After the incubation, the reading from the nutrient medium was performed, and the causes of urinary system infections and their sensitivity to antibiotics were determined.

RESULTS

Based on admitting diagnoses with suspected urinary system infection, microbiological examination of urine was negative in 58% of subjects, while in 42% of subjects urine culture was positive.

Table 1. Respondents whose urine cultures were positive by the place of residence

Place of Residence	Number	%
Orašje	64	60.38
Odžak	28	26.0
Domaljevac-Šamac	14	13.22
Overall:	106	100

Among the respondents with positive urine culture, there were 46 subjects or 43.4% of those with Escherichia coli, 23 subjects or 21.7% with Enterococcus faecalis, and Staphylococcus saprophyticus was

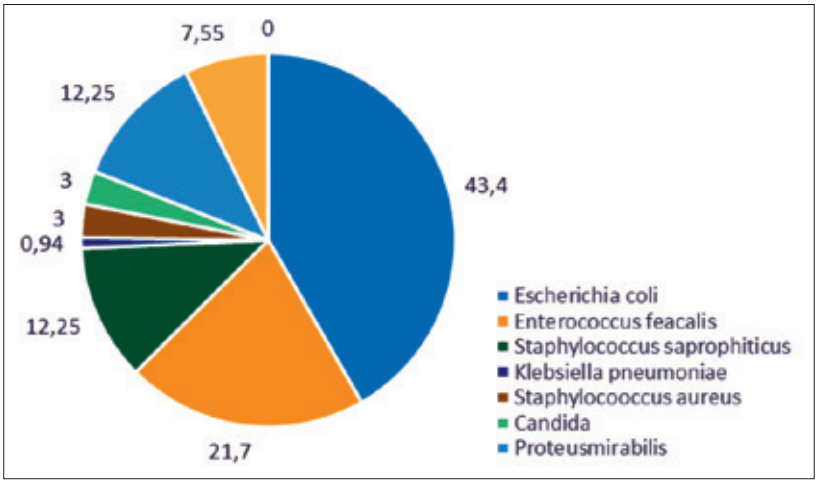

Figure 1. Incidence of individual causes of USI in subjects with positive urine culture

found in 13 subjects or 12.25%. Klebsiella pneumoniae was found in 1 subject or 0.94%, Staphylococcus aureus and Candida were found in 3% of subjects, Proteus mirabilis in 13 subjects or 12.25% and Pseudomonas aeruginosa in 8 subjects or 7.55% of respondents (Figure 1).

The study shows that inflammation of the bladder (N30) is the most common admitting diagnosis in subjects whose urine culture was positive. It occurred in as many as 50.5% of respondents. Urinary tract infection with unmarked location (N39.0) occurred in 26.7% of subjects, followed by acute cystitis (N30.0) in 6.9% of subjects. 5.9% of subjects were diagnosed with cystitis, unspecified (N30.9), 5% of subjects were referred with a diagnosis of second chronic cystitis (N30.2), while 4% of subjects reported interstitial cystitis (N30.1) and in 1% of subjects the admitting diagnosis there was second cystitis (N30.8) (Figure 2).

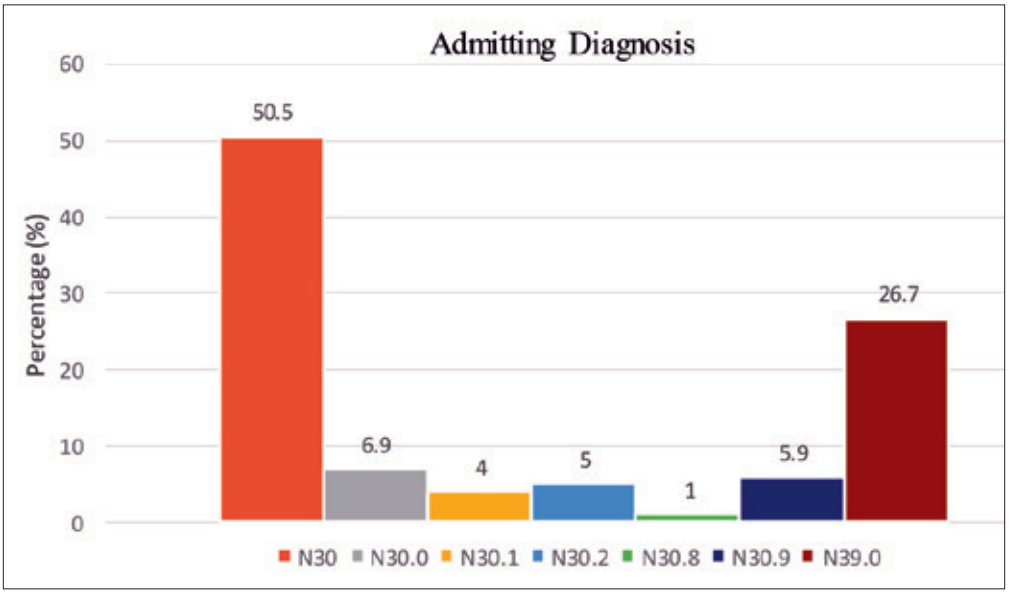

Figure 2. Frequency of Individual Admitting Diagnoses of Patients in Relation to Incidence

The subjects were divided into two groups, based on their age, and the analysis showed the association of the groups with individual causes of urinary system infection. (Table 2)

Table 2. Frequency distribution of causes in relation to the age of the respondents

Cause	Age of Respondents Number of Respondents (%)	
	18-34 yr.	35-50 yr.
Escherichiacoli	19 (41.30)	27 (58.70)
Enterococcusfaecalis	14 (60.87)	9 (39.13)
Klebsiella pneumoniae	0	1 (100.00)
Proteusmirabilis	7 (53.8)	6 (46.2)
Pseudomonas aeruginoza	4 (50.0)	4 (50.0)
Staphylococcusaureus	1 (100.0)	0
Staphylococcussaprophyticus	5 (38.40)	8 (61.60)
Candida	0	1 (100.0)

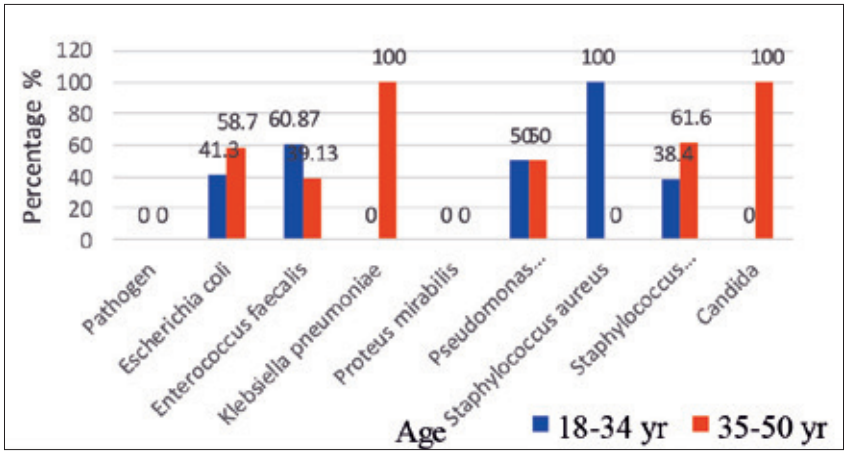

Figure 3. Frequency of Pathogens in Relation to the Respondents' Age

Table 3. Frequency of Positive Urine Culture Based on the Respondents' Age

Urine Culture Test	Age of Respondents Number of Respondents (%)	
	18-34	35-50
Positive	50 (47.15)	56 (52.85)
Negative	56 (39.40)	87 (60.60)

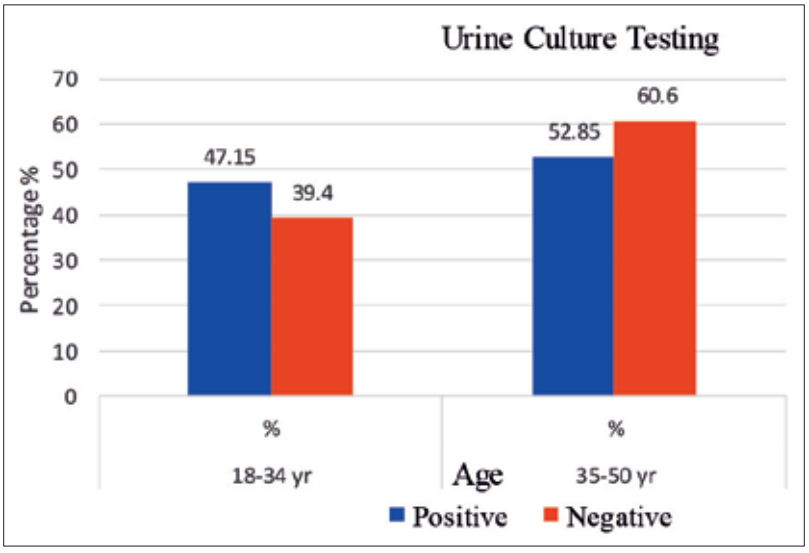

Figure 4. Frequency of Positive Urine Culture in Relation to Age

Table 4. AdmittingDiagnosesin Relation to Age

Admitting Diagnosis	Age of Respondents Number of Respondents (%)	
	18-34 yr.	35-50 yr.
Inflammation of the bladder (N30) - 53.80%	78 (58.10)	56 (41.90)
Acute cystitis (N30.0) 4.40%	2 (18.20)	9 (81.80)
Interstitial cystitis (N30.1) 4.40%	4 (40.00)	6 (60.00)
Second chronic cystitis (N30.2) 4.40%	1 (10.00)	9 (90.00)
Second cystitis (N30.8)	0	1 (100.00
Cystitis, unspecified (N30.9) 4.40%	2 (20.00)	8 (80.00)
Urinary tract infection, location unmarked (N39.0) 29.40%	19 (26.50)	54 (73.50)

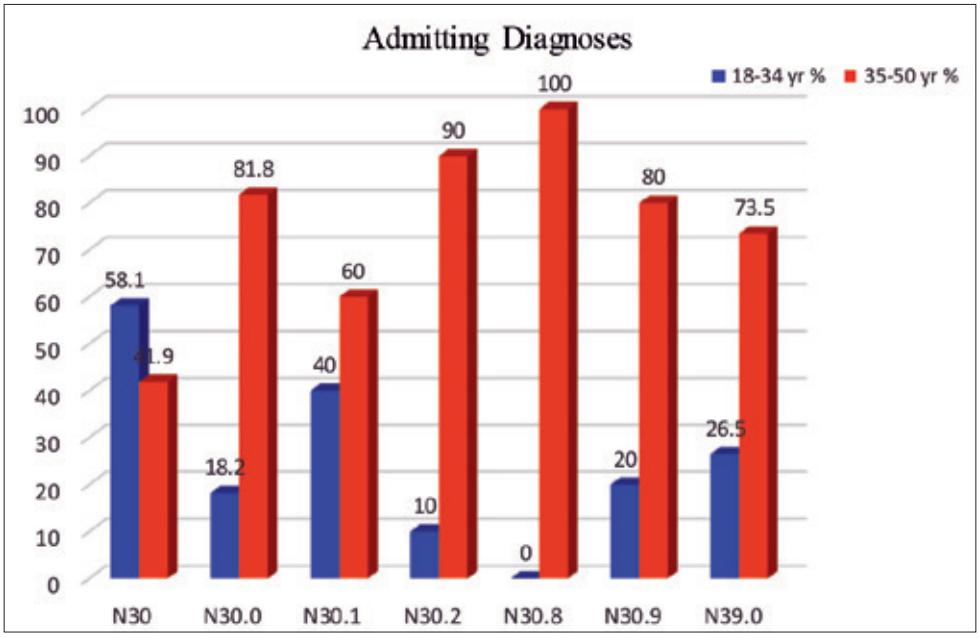

Figure 5. Admitting Diagnoses in Relation to Age

Table 5. Incidence of Individual Pathogens Depending on the Place of Residence.

Pathogen	Orašje (Number and %)	Odžak (Number and %)	Domaljevac -Šamac (Number and %)
Escherichia coli	28 (60.9)	13 (28.3)	5 (10.8)
Enterococcus feacalis	13 (56.6)	5 (21.7)	5 (21.7)
Klebsiella pneumoniae	1 (100.0)	0	0
Pseudomonas aeruginoza	4 (50.0)	4 (50.0)	0
Proteus mirabilis	6 (46.1)	5 (38.5)	2 (15.4)
Staphylococcus aureus	1 (100.0)	0	0
Staphylococcus saprophyticus	11 (84.6)	0	2 (15.4)
Candida	0	1 (100.0)	0

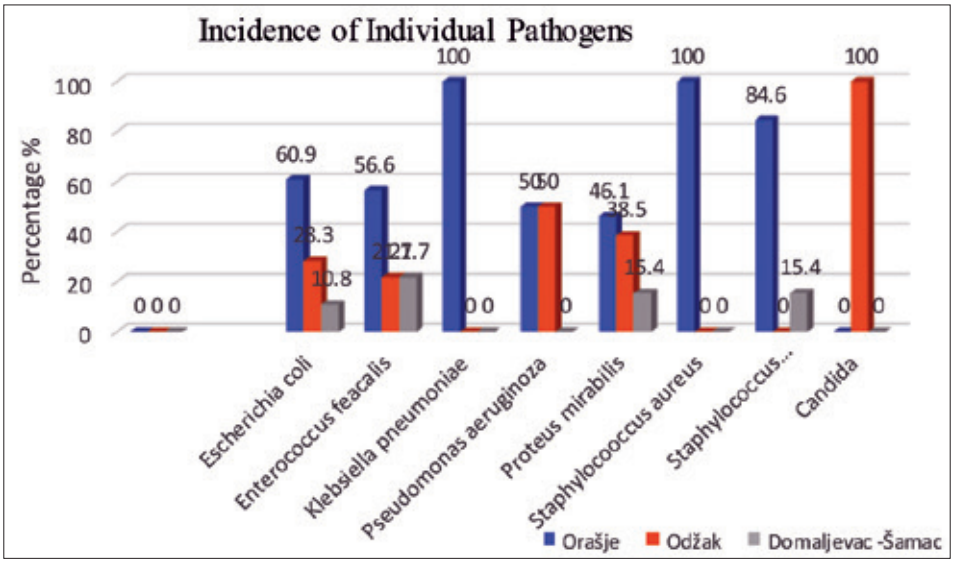

Figure 6. Incidence of Individual Pathogens Depending on the Place of Residence

Table 6. Distribution of Admitting Diagnoses Depending on the Place of Residence

Admitting Diagnosis	Orašje (Number and %)	Odžak (Number and %)	Domaljevac -Šamac (Number and %)
Inflammation of the bladder	79 (59.4)	38 (28.3)	17 (12.3)
Acute cystitis (N 30.0)	6 (54.5)	2 (18.2)	3 (17.3)
Interstitial cystitis (N 30.1)	8 (80.0)	2 (20.0)	0
Second chronic cystitis (N30.2)	5 (50.0)	4 (40.0)	1 (10.0)
Second cystitis (N30.8)	1 (100.0)	0	0
Cystitis, unspecified (N30.9)	6 (60.0)	2 (20.0)	2 (20.0)
Urinary tract infection, location unmarked (N39.0)	38 (52.9)	24 (32.3)	11(14.8)

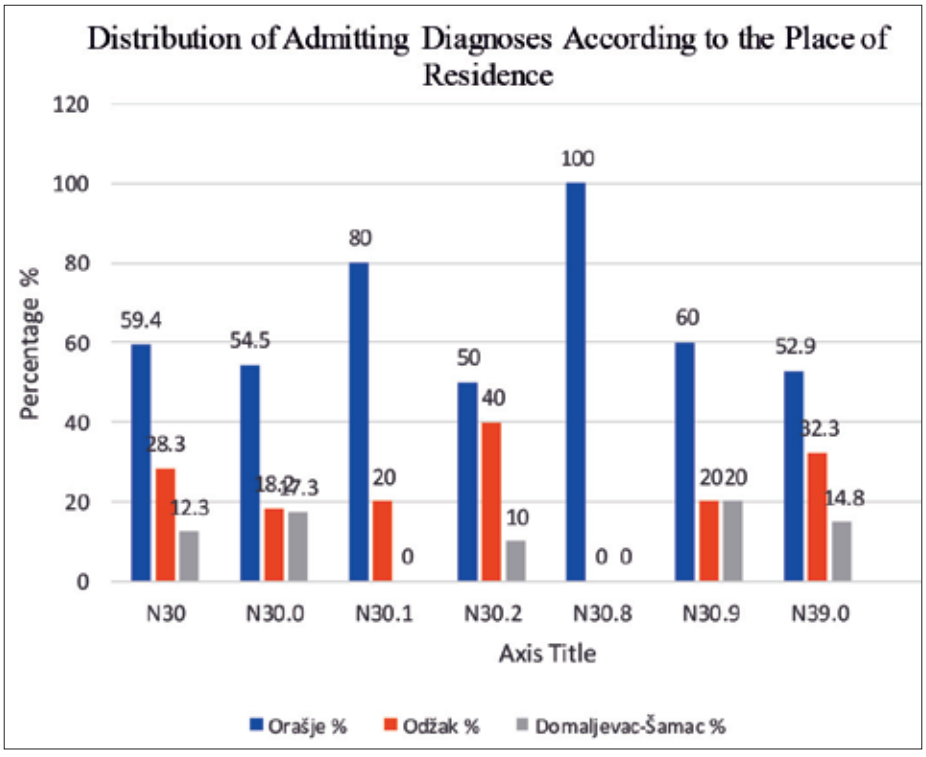

Figure 7. Distribution of Admitting Diagnosis According to the Place of Residence

Table 7. Frequency of Confirmed USIs Based on the Respondents' Place of Residence.

Urine Culture Test	Orašje (Number and %)	Odžak (Number and %)	Domaljevac-Šamac (Number and %)
Positive	64 (60.4)	28 (26.4)	14 (13.2)
Negative	87 (60.8)	39 (27.2)	17 (12.0)

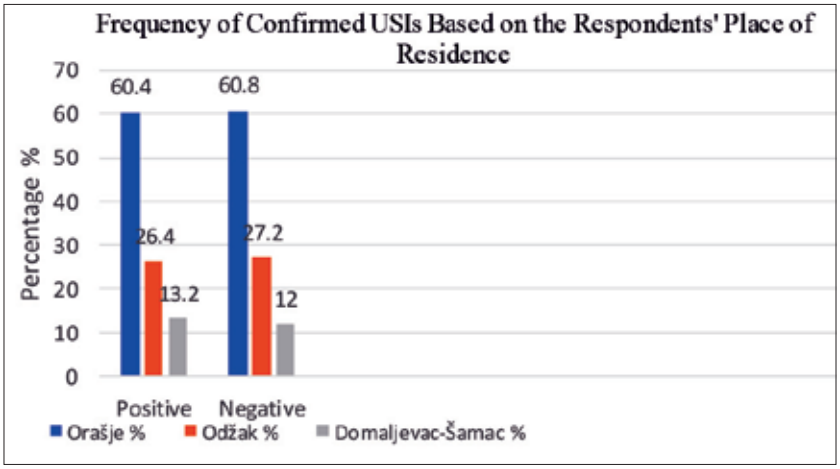

Figure 8. Frequency of Confirmed USIs Based on the Respondents' Place of Residence

DISCUSSION

Previous research and observations have shown that urinary system infections are more prevalent or more common in females. Some research has shown that due to hormonal status as well as evident anatomical differences compared to men, women are up to 30 times more likely to have urinary system infections.

For this reason, our research included female population. Microbiological analysis of urine showed that 42.57% of urine cultures were positive, while in 57.43% of respondents the test result was negative.

Also, scientific research shows that the development of urinary system infections increases by 7% in older women compared to women aged 18 to 50. Considering that in the research we divided women of reproductive age into two groups according to age: respondents aged 18 to 34 and respondents aged 35 to 50. The results confirmed that the respondents from the older group were more often referred for microbiological examination, thus making up a total of 52.85% of respondents with positive tests.

This result was in line wirh previously published results and conclusions in the literature, which showed that the risk of urinary tract infection increases with age. A study was conducted in France (Francis et al.) during 2016, in which a significant susceptibility of women to urinary system infections was found.

Our research found Escherichia coli in 43.4% of positive tests or out of a total of 106 responendts with positive tests, in 46 subjects this bacteria was present; therefore it is by far the most common cause. This result coincides with the results of research published in the literature. In 2018, Schreiber et al found that Escherichia coli is the most common pathogen causing USI in the United States and Europe. Furthermore, a study conducted in France in 2016 showed that the most common bacteria that causes urinary tract infections are: E. coli, Enterococcus faecalis, Staphylococcus saprophyticus, Klebsiella pneumoniae, Proteus mirabilis, and Pseudomonas aeruginosa.

According to independent research, the most common diagnosis of urinary tract infections is cystitis. These statements agree with the results obtained in our study, in which of all the observed diagnoses observed, the most common is bladder inflammation or cystitis (N30), in 53.80% or in 134 of the 249 surveyed.

In addition to the fact that individual age groups were associated with infectious agents, each age group was also associated with admitting diagnoses. In this case, a statistically significant association was found between admitting diagnoses and the age group of respondents aged 35 to 50. Furthermore, this study showed that infections were more prevalent in older subjects, aged 35 to 50, compared to younger subjects.

This analysis can serve as a good basis for new research.

CONCLUSIONS

- The frequency of urinary system infections in women of reproductive age from the area of the three municipalities of Posavina County (Orašje, Odžak and Domaljevac-Šamac) is 42.57%. The sample included 249 women, 106 of whom had a positive urine culture.
- In the observed sample, it is evident that the most common cause of urinary tract infections is Escherichia coli, which is present in 43.4% of total positive urine cultures, or 46 cases of Escherichia coli infections out of a total of 106 positive urine cultures.
- Reviewing referrals from family doctors, it was established that the most common admitting diagnosis was cystitis - inflammation of the bladder (N30) - 53.80%.
- The subjects of the older age group (35 to 50 year olds) were proven to be more susceptible to urinary tract infections.

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Professional paper

Analysis of Modern Hepatitis C Control Effects

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ABSTRACT: Viral hepatitis C (hep C, HCV) most commonly occurs in the age group of 30 to 49. Initially, the dominant group consisted of middle-aged patients infected through blood transfusion. Recently, an increase in HCV has been observed among patients of younger age.
Today, the main risk group consists of intravenous drug users (IVDUs) with a prevalence of 80%, and the infection normally occurs very soon after starting to take intravenous drugs. Hepatitis C viral infection is also associated with cocaine/heroin consumption, and the infection occurs as a result of the use of common blood-contaminated equipment.
In the presented research, the largest number of patients is between the ages of 30 and 40. In 36 patients, a stable virological response was achieved, i.e. 90%, while most of these patients were previously treated with some other treatment modalities.
Since the therapeutic possibilities are limited and there is no vaccine, prevention plays a key role in the eradication of HCV infection. Eradication and health education of the population are needed, with the aim of acquiring knowledge about possible ways of infection transmission, and thus the possibilities of protection against infection.

Keywords: Hepatitis C, prevalence, viruses, education.

INTRODUCTION

Chronic hepatitis C is defined as chronic liver inflammation (lasting more than six months) which is caused by the hepatitis C virus (HCV). Until 1989, when this virus was discovered, it was called non-A non-B. This infection is a significant global health problem with a wide range of health, social and economic consequences. (Vukobrat-Bijedić, 2008).

Acute hepatitis C has an asymptomatic course in most patients, so it is rarely recognised and occurs mostly in anicteric form. Chronic hepatitis is in many cases also asymptomatic, or is manifested only by chronic fatigue. Hepatitis C viral infection also affects the quality of life because there is weakness, muscle pain, pain below the right costal margin, which result in reduced physical, emotional and social functioning (Verhaz, 2012).

HCV infection has characteristics of a silent epidemic in the world today. According to the latest estimates of the World Health Organisation, the global prevalence of HCV based on HCV antibodies is 1.6% (1.3% - 2.1%), which corresponds to 115 million (range: 92-149 million) patients. Of that number, about 350,000-500,000 people die every year from HCV-related liver disease and its complications. Hepatitis C virus is the cause of about 40% of all chronic liver diseases in the United States, and HCV-related cirrhosis is the most common indication for liver transplantation among the adult population (WHO, 2021).

To address the issue of people with hepatitis, the WHO accepted the initiative of the World Hepatitis Alliance and confirmed 28 July, as a date when by numerous activities around the world it is pointed to the importance of prevention, care and finding new drugs to cure and eradicate diseases caused by this virus. The introduction of mandatory blood testing for hepatitis C viral antibodies (anti-HCV) has reduced the number of post-transfusion viral infections and ranges within risk limits of up to 1: 200,000. However, the number of patients has not decreased, as other modes of transmission such as intravenous drugs have

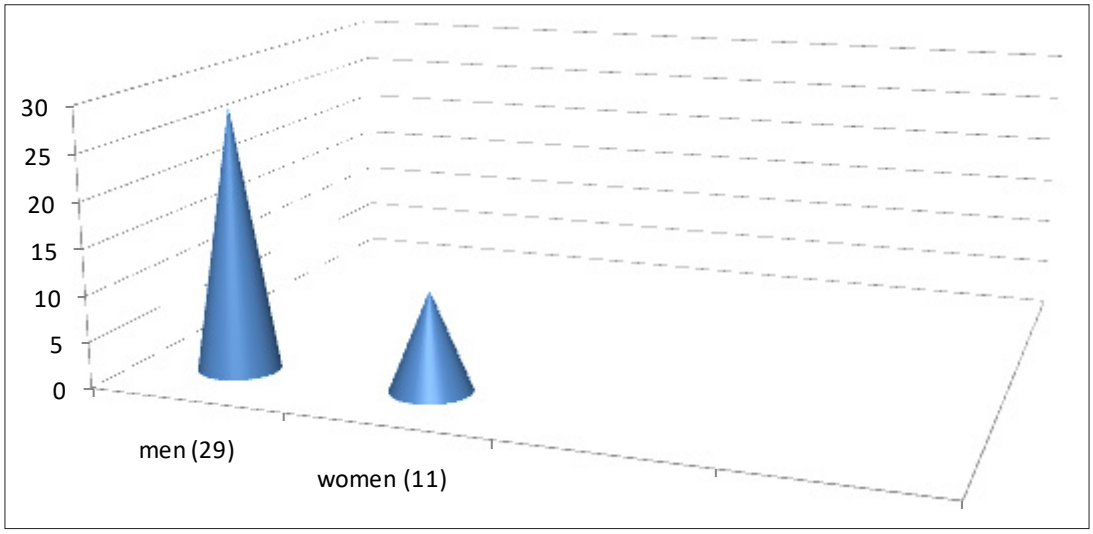
become important. Although little has been achieved in the primary prevention of hepatitis C through the vaccine, great progress has been made in the treatment of HCV patients with over 90% cured according to the latest treatment protocols.

MATERIALS AND METHODS

- Forty patients with chronic hepatitis C treated with interferon free therapy were monitored. In all the diseased the diagnosis was made on the basis of clinical, laboratory, radiological and patho-histological findings.
- The study included patients in hospital treatment at the Clinic for Infectious Diseases in the period from 1 January to 31 December 2019.
- A retrospective-descriptive-epidemiological method was used in the paper. The obtained data were processed in absolute and relative numbers and presented graphically.

RESULTS

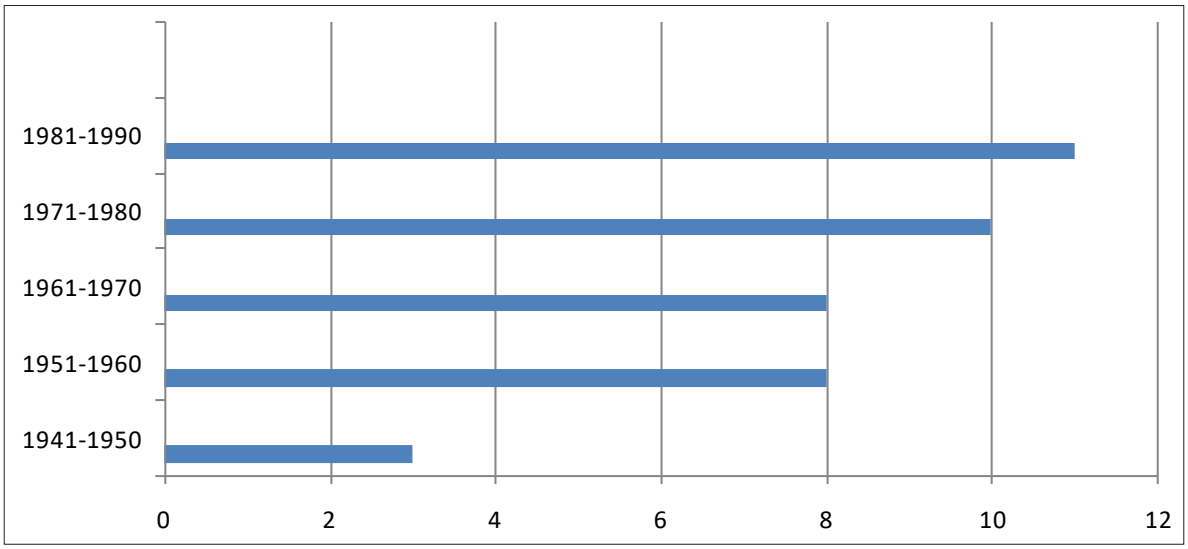
Graph 1. Graphic representation of treated patients by sex.



From Graph 1 we see that in the observed period, the number of men significantly dominate over that of females.

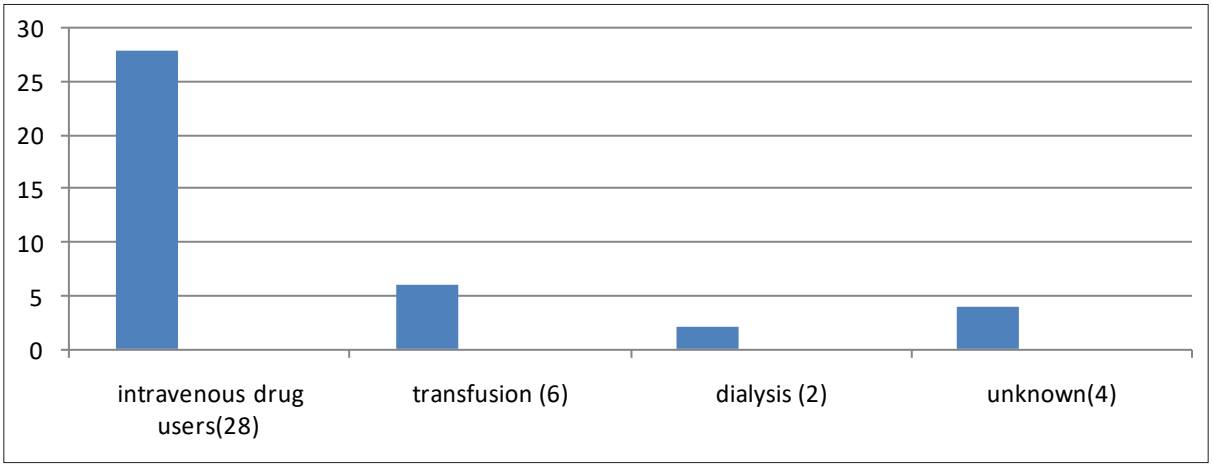
A total of 29 or 72.5% of men were treated in the observed time period, while only 11 or 27.5% were women.

Graph 2. Graphic representation of the prevalence of chronic hepatitis C (CHC) patients by age.



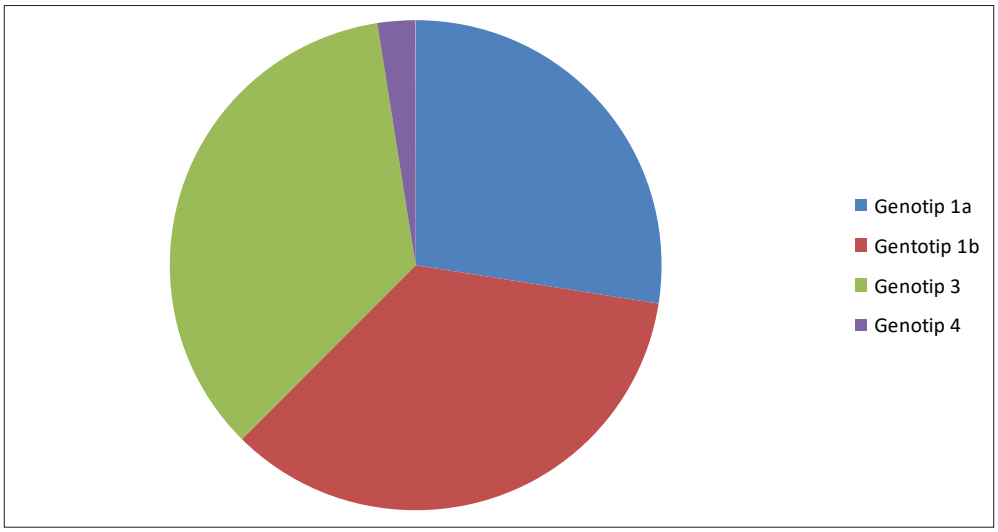
In the graph shown, we see that in the observed period, the largest number of patients was born between 1981 and 1990. Eleven patients were ages born between 1981 and 1990 or 27.5%, while the number of patients born between 1971 and 1980 was 10 or 25%; then those born from 1961 to 1970 and 1951 to 1960 were 8 patients or 20%, while only 3 patients or 7.5% were from the age group born from 1940 to 1950.

Graph 3. The graph shows the number of the diseased in relation to the mode of transmission



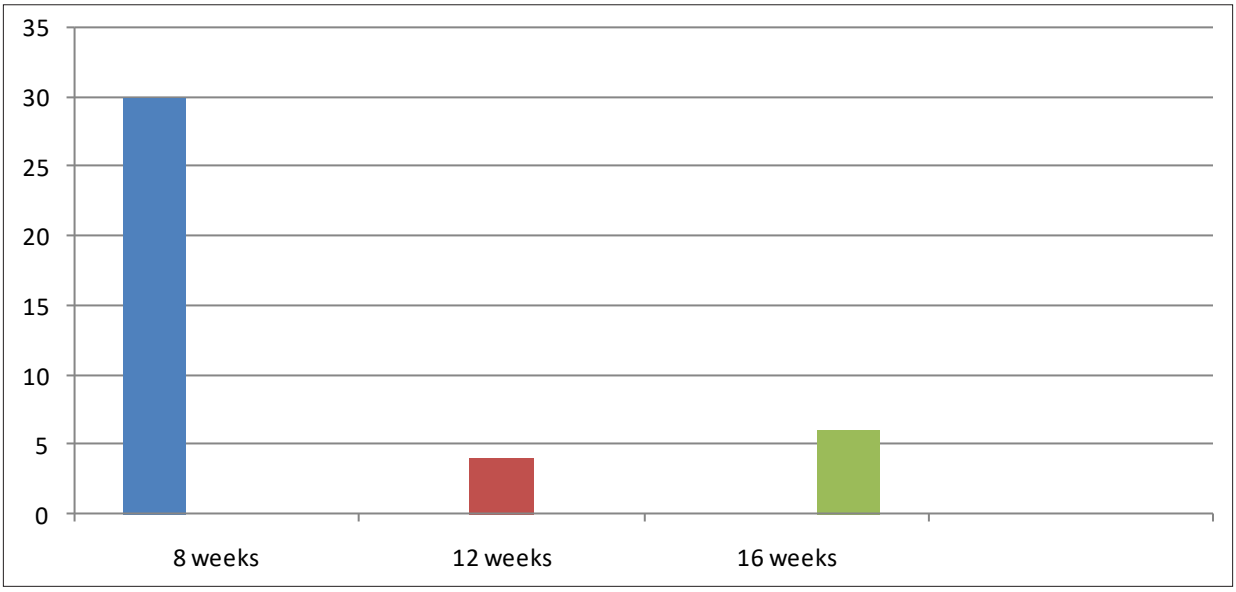
The graph shows that the largest number of patients was from the population of intravenous drug users - 28 or 70%, 6 patients or 15% became infected during blood transfusion, 2 patients or 5% by dialysis, while 4 patients or 10% have an unknown way of transmission.

Graph 4. Graphic display of genotype representation



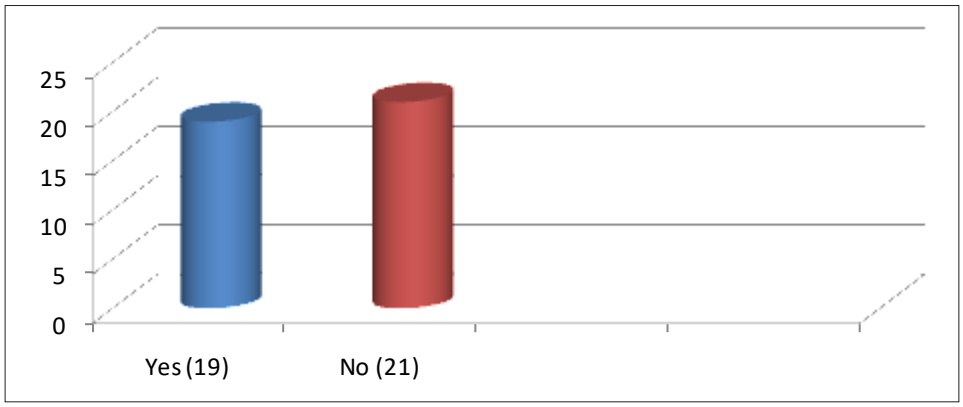
In the graph shown, we see that there were the same numbers of patients with genotype 1 b and 3 or 14 patients (35%), with genotype 1 a 11 patients or 27.5%, and genotype 4 - 1 patient or 2.5%.

Graph 5. Graphic representation of the therapy duration



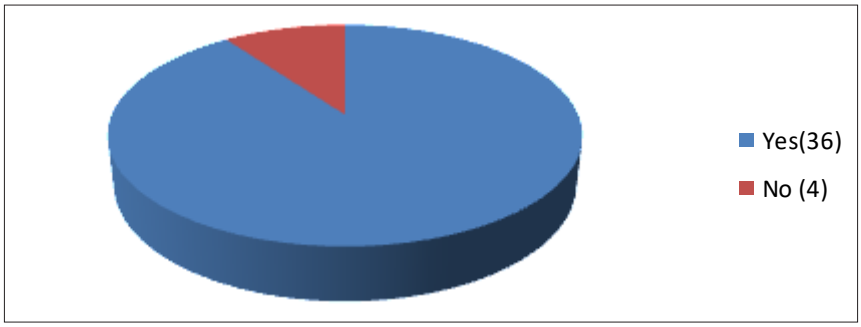
The graph shows that the largest number of patients was treated for 8 weeks - 30 patients or 75%, 6 patients or 15% for 16 weeks, while 4 patients or 10% were treated for 12 weeks.

Graph 6. Graphic presentation of previously treated patients with some of the treatment modalities



In the graph shown, we see that 19 patients or 47.5% had been previously treated with some form of therapy, while 21 or 52.5% had not been treated.

Graph 7. Graphic presentation of patients who achieved a stable virological response after therapy



In the graph shown, we see that 36 patients or 90% had a stable virological response, while 4 or 10% did not have a stable virological response.

DISCUSSION

Infection by hepatitis C virus is widespread in the world. It is estimated that about 170 million people in the world (1-5% of the population in different countries) are chronically infected with viral hepatitis C, because as many as 85-90% of acute infections with this virus become chronic, 25-35% develop liver cirrhosis, and 1% - 5% also develop hepatocellular carcinoma.

The prevalence of HCV infection is 0.04% to 14.5% depending on the geographical area. The lowest prevalence was found in Western European countries, and Canada and Australia as well. Central Europe and the United States have a slightly higher propagation (Delić, 2012).

Mediterranean countries have the highest prevalence of HCV infection in Europe, ranging from 0.7% in Italy to 0.9% in Spain. In South America the prevalence is from 0.9% in Argentina to 1.75% in Brazil. In Asia the prevalence is 1.5%, in Japan up to 2.5%. The highest prevalence is in the countries of North and Central Africa, especially Egypt, where the prevalence is from 13% to 20% (Krkić-Dautović Sajma, 2011).

According to the official data of the Institute of Public Health of the Republic of Srpska, in 2014, 47 patients with the hepatitis C virus were registered, with an incidence rate of 3.4/100,000, and one death was registered. In the last five years, the incidence rate has been fairly uniform, and ranged from 2.7 to 3.8 per 100,000 inhabitants.

The disease most often occurs in the age group of 30 to 49. Initially, the dominant group consisted of middle-aged patients infected by blood transfusion. Recently, there has been an increase in CHC at a younger age, and it is associated with an increase in intravenous drug addiction (Kostić, 2005).

Today, the main risk group is intravenous drug users (IVDUs) with a prevalence of 80%, and the infection usually occurs very soon after the start of intravenous drug use.

Our paper confirms the global trend, where out of 40 patients, 28 were intravenous drug users.

CONCLUSION

About 170 million people worldwide are infected with the hepatitis C virus. In the past, the dominant group consisted of patients who became infected through blood transfusions, while today the main risk group consists of intravenous drug users, as is the case in this paper where out of 40 patients, 28 were intravenous drug users. Possible, but rare modes of transmission are home contact, sexual contact, and perinatal transmission.

Acute HCV infection most commonly occurs as an asymptomatic disease and about 80% of patients develop a chronic infection that is mostly discovered by chance. Significant predisposing factors for the development of progressive liver disease are old age, male gender and excessive alcohol consumption.

One of the most common genotypes is genotype 3, which is associated with intravenous drug use, which has been proven in this paper as the most common route of transmission The largest number of patients are males, i.e. 29 people or 72.5%.

A stable virological response was achieved in 36 patients, i.e. 90%, while most of these patients had been previously treated with some other treatment modalities.

Since the therapeutic possibilities are limited, and there is no vaccine, prevention plays a key role in the eradication of HCV infection. Eradication and health education of the population is needed, with the aim of acquiring knowledge about possible ways of transmitting the infection, and thus the possibilities of protection against infection.

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