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LOWER URINARY TRACT SYMPTOMS AND DEPRESSION IN PATIENTS WITH MULTIPLE SCLEROSIS

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SUMMARY

Background: *Both depression and lower urinary tract symptoms (LUTS) may be present in patients with multiple sclerosis (MS). The objective of this study was to give an insight on depression and LUTS in patients with MS in Croatia and to determine the possible association between LUTS and depression in patients with MS.*

Subjects and methods: *This was a prospective cross-sectional study conducted in a tertiary healthcare center in Croatia. Hundred and one consecutive patients with MS (75 female, 26 male, mean age 42.09 (range 19-77) years, mean Expanded Disability Status Scale (EDSS) score 3.1 (range 0.0-7.0)) participated in this study. We evaluated LUTS and related quality of life (QoL) using three International Consultation on Incontinence Questionnaires (ICIQ) enquiring about overactive bladder (ICIQ-OAB), urinary incontinence short form (ICIQ-UI SF) and lower urinary tract symptoms related quality of life (ICIQLUTS-QoL). ICIQ-OAB and ICIQLUTS-QoL were for this purpose with permission successfully translated and validated into Croatian, while ICIQ-UI SF was already previously validated for the Croatian language. Information regarding treatment for depression was obtained during the medical interview. Data were analyzed and interpreted using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA).*

Results: *89.10% (N=90) patients with MS reported urgency with urge urinary incontinence (UUI) present in 70.29% (N=71). 81.18% (N=82) patients reported nocturia, and 90.09% (N=91) reported feeling drowsy or sleepy during the day due to bladder symptoms. Neurological deficit measured by EDSS was found to positively correlate with LUTS on all three questionnaires: ICIQ-OAB ($r=0.390$, $p<0.05$), ICIQ-UI SF ($r=0.477$, $p<0.01$) and ICIQ-LUTSQoL ($r=0.317$, $p<0.05$). 25 patients were in treatment for depression. There were no significant differences between female and male patients regarding treatment for depression ($\chi^2=0.018$, $df=1$, $p>0.05$). Results on ICIQ-UI SF showed that depressive patients had more pronounced LUTS ($t=2.067$, $df=99$, $p<0.05$), which was also true for the ICIQ-LUTSQoL ($t=-2.193$, $df=99$, $p<0.05$). Positive correlations were found between depression and LUTS on ICIQ-UI SF ($r=0.203$, $p<0.05$) and ICIQ-LUTSQoL ($r=0.215$, $p<0.05$).*

Conclusion: *This study gives insight into the presence of depression and LUTS in Croatian patients with MS for which purpose ICIQ-OAB and ICIQ-LUTSQoL were with permission successfully translated and validated into Croatian. The connection between depression and LUTS must be considered when managing patients with MS.*

Key words: *lower urinary tract symptoms (LUTS) – depression - multiple sclerosis (MS) - International Consultation on Incontinence Questionnaires (ICIQ) - overactive bladder (OAB) - quality of life (QoL)*

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INTRODUCTION

Multiple sclerosis (MS) is a chronic neurodegenerative demyelinating disease that affects the central nervous system (CNS). Both depression and lower urinary tract symptoms (LUTS) may be present in patients with MS. Recent review highlighted a complex relation between depression and MS with the involvement of the limbic

system, the role of the hippocampus and the impact of brain lesions on the emotional status of MS patients (Corallo et al. 2019).

Although commonly experienced in MS patients, LUTS are largely undiagnosed and untreated (Khalaf et al. 2015). Usually, patients report overactive bladder (OAB) symptoms (urgency, incontinence, frequent voiding and nocturia), as well as the inability to initiate voiding voluntarily, while typical findings on urodynamics include the presence of detrusor overactivity (DO), detrusor sphincter dyssynergia (DSD) and detrusor underactivity (DU) (Stoffel 2017; Tudor et al. 2016). If LUTS are neglected, they may result in different complications as well as affect patient's general condition and Quality of life (QoL) (Castel-Lacanal et al. 2015; Tornic & Panicker 2018; Coyne et al. 2002).

Recent analysis showed that the overall MS prevalence rate in Croatia is 143.8 per 100 000 population (6160 patients identified, majority - 72% women) (Benjak et al. 2018), while recent joint study in the region found depression in 54.7% of patients with MS (mild - 17.9%; mild to moderate - 12.9%; moderate to severe - 23.9%) (Drulovic et al. 2015). The epidemiological data on the prevalence of LUTS in MS patients in Croatia is however lacking.

The objective of this study was to give an insight on depression and LUTS in patients with MS in Croatia and to determine the possible association between LUTS and depression in patients with MS.

SUBJECTS AND METHODS

This was a prospective cross-sectional study conducted in a tertiary healthcare center in Croatia over 10 months. The research was approved by the local Ethics Committee.

LUTS and related QoL in patients with multiple MS were evaluated using International Consultation on Incontinence Questionnaires (ICIQ): International Consultation on Incontinence Questionnaire Overactive Bladder (ICIQ-OAB) (Donovan et al. 1996, Jackson et al. 1996), International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UI SF) (Avery et al. 2004) and International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Quality of Life (ICIQLUTS-QoL) (Avery et al. 2004, Donovan et al. 1996, Jackson et al. 1996, Kelleher et al. 1997, Nystrom et al. 2015). For this purpose, ICIQ-OAB and ICIQLUTS-QoL were with permission translated into Croatian and validated, while ICIQ-UI SF was already previously validated for the Croatian language. ICIQ-OAB and ICIQLUTS-QoL were initially translated into Croatian then back-translated to English. Back translated versions were reviewed by the ICIQ group and necessary adjustments were made. The Croatian versions of all the questionnaires were then piloted on ten patients (there were no questions or instructions that were found confusing).

ICIQ-OAB is a 4-item questionnaire that has two parts, part A enquires about urgency, frequency, nocturia, urgency leakage (score 0-16), and part B about bother related to OAB (score 0-40). ICIQ-LUTS-QoL also consists of two parts, part A enquires about quality of life (score 0-76), and part B about related bother (score 0-200). ICIQ-UI SF consists of 6 questions and inquires about urinary incontinence.

Information on treatment for depression was obtained during the medical interview.

Data were analyzed and interpreted using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA) and a p-value<0.05 was considered to be significant.

Table 1. Internal consistency (reliability) was found to be very high for ICIQ-OAB (α=0.898)

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
3a. How often do you pass urine during the day?	27.7253	289.179	0.622	0.897
3b. How much does this bother you? Please ring a number between 0 (not at all) and 10 (a great deal)	23.8242	215.591	0.848	0.869
4a. During the night, how many times do you have to get up to urinate, on average?	27.4396	293.738	0.607	0.900
4b. How much does this bother you? Please ring a number between 0 (not at all) and 10 (a great deal)	24.1758	215.658	0.787	0.877
5a. Do you have to rush to the toilet to urinate?	26.6044	284.486	0.793	0.892
5b. How much does this bother you?	23.0769	206.227	0.907	0.862
6a. Does urine leak before you can get to the toilet?	27.3956	287.420	0.743	0.894
6b. How much does this bother you?	22.9890	203.833	0.817	0.877

* ICIQ-OAB - International Consultation on Incontinence Questionnaire Overactive Bladder

RESULTS

Hundred and one consecutive patient with MS (75 female, 26 male, mean age 42.09 (range 19-77) years, mean Expanded Disability Status Scale (EDSS) score 3.1 (range 0.0-7.0), 95 patients with relapse remitting MS (RRMS), 5 secondary progressive MS (SPMS), and one patient with primary progressive MS (PPMS)) participated in this study.

Validation of the ICIQ-OAB and ICIQ-LUTSQoL showed favourable results. Internal consistency (reliability) was found to be very high for both ICIQ-OAB (α=0.898) (Table 1) and ICIQ-LUTSQoL (α=0.967) (Table 2). Stability (test-retest reliability) was found to be very high for ICIQ-OAB part a (r=0.984, p<0.001) (Table 3) and ICIQ-OAB part b (r=0.991, p<0.001) (Table 4). Content/face validity was found to be good (Table 5 and Table 6).

Table 2. Internal consistency (reliability) was found to be very high for ICIQ-LUTSQoL (α=0.967)

Item-Total Statistics During the past four weeks, how often have your bladder symptoms…	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
3. Made you carefully plan your journey?	75.36	961.804	0.777	0.965
4. Caused you to feel drowsy or sleepy during the day?	75.35	989.360	0.600	0.966
5. Caused you to plan "escape routes" to toilets in public places?	75.30	970.028	0.758	0.965
6. Caused you distress?	75.68	975.942	0.698	0.966
7. Frustrated you?	75.73	975.092	0.740	0.965
8. Made you feel like there is something wrong with you?	75.63	980.325	0.619	0.966
9. Interfered with your ability to get a good night's rest?	75.76	977.075	0.643	0.966
10. Caused you to decrease your physical activities (exercising, sports, etc.)?	75.44	979.622	0.601	0.966
11. Prevented you from feeling rested upon waking in the morning?	75.54	973.210	0.658	0.966
12. Frustrated your family and friends?	75.85	977.200	0.700	0.966
13. Caused you anxiety or worry?	75.62	968.061	0.772	0.965
14. Caused you to stay home more often than you would prefer?	75.65	980.515	0.554	0.967
15. Caused you to adjust your travel plans so that you are always near a toilet?	75.36	955.013	0.840	0.964
16. Made you avoid activities away from toilets (i.e., walks, running, hiking)?	75.36	953.557	0.802	0.965
17. Made you frustrated or annoyed about the amount of time you spend in the toilet?	75.71	967.699	0.820	0.965
18. Awakened you during sleep?	75.61	974.931	0.756	0.965
19. Made you worry about odour or hygiene?	75.56	961.927	0.714	0.965
20. Made you uncomfortable while travelling with others because of needing to stop for a toilet?	75.84	964.735	0.761	0.965
21. Affected your relationships with family and friends?	76.22	974.713	0.753	0.965
22. Caused you to decrease participating in social gatherings, such as parties or visits with family or friends?	75.76	955.884	0.819	0.965
23. Caused you embarrassment?	75.70	960.027	0.816	0.965
24. Interfered with getting the amount of sleep you needed?	75.71	965.281	0.803	0.965
25. Caused you to have problems with your partner or spouse?	76.08	974.651	0.637	0.966
26. Caused you to plan activities more carefully?	75.51	957.126	0.893	0.964
27. Caused you to locate the closest toilet as soon as you arrive at a place you have never been?	75.27	956.104	0.806	0.965
28. Overall, how much do your urinary symptoms interfere with your everyday life?	72.90	860.735	0.798	0.969

*ICIQ-LUTSQoL - International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Quality of Life

Table 3. Stability (test-retest reliability) was found to be very high for ICIQ-OAB part a (r=0.984, p<0.001)

		Correlations	
		ICIQ-OAB part a_1_mean	ICIQ-OAB part a_2_mean
ICIQ-OAB part a_1_mean	Pearson Correlation	1	*0.984***
	Sig. (2-tailed)		0.000
	N	23	23
ICIQ-OAB part a_2_mean	Pearson Correlation	0.984**	1
	Sig. (2-tailed)	0.000	
	N	23	23

*ICIQ-OAB - International Consultation on Incontinence Questionnaire Overactive Bladder;
** Correlation is significant at the 0.01 level (2-tailed)

Table 4. Stability (test-retest reliability) was found to be very high for ICIQ-OAB part b (r=0.991, p<0.001)

		Correlations	
		ICIQ-OAB part b_1_mean	ICIQ-OAB part b_2_mean
ICIQ-OAB part b_1_mean	Pearson Correlation	1	*0.991***
	Sig. (2-tailed)		0.000
	N	23	23
ICIQ-OAB part b_2_mean	Pearson Correlation	0.991**	1
	Sig. (2-tailed)	0.000	
	N	23	23

*ICIQ-OAB - International Consultation on Incontinence Questionnaire Overactive Bladder;
** Correlation is significant at the 0.01 level (2-tailed)

Table 5. Content/face validity on ICIQ-OAB was found to be good

ICIQ-OAB	Valid	Missing
3a	101	0
3b	98	3
4a	101	0
4b	98	3
5a	100	1
5b	96	5
6a	99	2
6b	96	5

*ICIQ-OAB - International Consultation on Incontinence Questionnaire Overactive Bladder (questions correspond to those listed in the Table 1)

Results on ICIQ-OAB, ICIQ-LUTSQoL and ICIQ-UI SF are in detail presented in Table 7. Symptoms that were reported to be most bothersome on ICIQ-OAB were urgency and urge urinary incontinence (UUI) - average response was 6.14±3.78 for urgency, and 6.11±4.21 for UUI on a scale 0 (not at all) - 10 (a great deal). On ICIQ-LUTSQoL overall, on a scale 0 (not at all) - 10 (a great deal), patients with MS report their urinary symptoms to interfere with their everyday life on average 5.79±3.49 (range 0-10). On ICIQ-UI SF 70.29% (N=71) patients with MS report incontinence, with 61.38% (N=62) experiencing a fair amount of urine leakage. It occurs most often (25.74%, N=26) several times a day. On ICIQ-UI SF overall, on a scale 0 (not at all) - 10 (a great deal), patients with MS report their urinary symptoms to interfere with their everyday life on average 4.92±3.98 (range 0-10). Mean sum score on ICIQ-UI SF was 9.04±6.73 (range 0-20).

Table 6. Content/face validity on ICIQ-LUTSQoL was found to be good

ICIQ-LUTSQoL	Valid	Missing
3	101	0
4	101	0
5	101	0
6	101	0
7	101	0
8	101	0
9	100	1
10	101	0
11	101	0
12	101	0
13	101	0
14	101	0
15	101	0
16	101	0
17	99	2
18	101	0
19	99	2
20	101	0
21	100	1
22	100	1
23	100	1
24	100	1
25	97	4
26	99	2
27	98	3
28	99	2

*ICIQ-LUTSQoL - International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Quality of Life (questions correspond to those listed in the Table 2)

Table 7. Lower urinary tract symptoms (LUTS) and their impact on quality of life (QoL) assessed by International Consultation on Incontinence Questionnaires (ICIQ): ICIQ-OAB, ICIQ-UI SF and ICIQLUTS-QoL

ICIQ-OAB	(…on average, over the *past four weeks*)	
	3a. How often do you pass urine during the day? (>than 8 times - responses from 2-4)	35.64% (N=36)
	4a. During the night, how many times do you have to get up to urinate, on average? (the need for an individual to wake up at night one or more times to void - responses from 1-4)	81.18% (N=82)
	5a. Do you have to rush to the toilet to urinate? (responses from 1-4)	89.10% (N=90)
	6a. Does urine leak before you can get to the toilet? (responses from 1-4)	70.29% (N=71)
ICIQ-LUTSQoL	*During The Past Four Weeks, How Often Have Your Bladder Symptoms…* (responses from 2-6)	
	3. Made you carefully plan your journey?	76.23% (N=77)
	4. Caused you to feel drowsy or sleepy during the day?	90.09% (N=91)
	5. Caused you to plan "escape routes" to toilets in public places?	86.13% (N=87)
	6. Caused you distress?	76.23% (N=77)
	7. Frustrated you?	75.24% (N=76)
	8. Made you feel like there is something wrong with you?	76.23% (N=77)
	9. Interfered with your ability to get a good night's rest?	70.29% (N=71)
	10. Caused you to decrease your physical activities (exercising, sports, etc.)?	74.25% (N=75)
	11. Prevented you from feeling rested upon waking in the morning?	75.24% (N=76)
	12. Frustrated your family and friends?	71.28% (N=72)
	13. Caused you anxiety or worry?	74.25% (N=75)
	14. Caused you to stay home more often than you would prefer?	73.26% (N=74)
	15. Caused you to adjust your travel plans so that you are always near a toilet?	73.26% (N=74)
	16. Made you avoid activities away from toilets (i.e., walks, running, hiking)?	73.26% (N=74)
	17. Made you frustrated or annoyed about the amount of time you spend in the toilet?	73.26% (N=74)
	18. Awakened you during sleep?	85.14% (N=86)
	19. Made you worry about odour or hygiene?	73.26% (N=74)
	20. Made you uncomfortable while travelling with others because of needing to stop for a toilet?	65.34% (N=66)
	21. Affected your relationships with family and friends?	60.39% (N=61)
	22. Caused you to decrease participating in social gatherings, such as parties or visits with family or friends?	67.32% (N=68)
	23. Caused you embarrassment?	70.29% (N=71)
	24. Interfered with getting the amount of sleep you needed?	71.28% (N=72)
	25. Caused you to have problems with your partner or spouse?	54.45% (N=55)
	26. Caused you to plan activities more carefully?	74.25% (N=75)
	27. Caused you to locate the closest toilet as soon as you arrive at a place you have never been?	78.21% (N=79)
ICIQ-UI SF	(…on average, over the *past four weeks*)	
	6. When does urine leak?	
	never – urine does not leak n=21	
	leaks before you can get to the toilet n=52	
	leaks when you cough or sneeze n=29	
	leaks when you are asleep n=10	
	leaks when you are physically active/exercising n=18	
	leaks when you have finished urinating and are dressed n=18	
	leaks for no obvious reason n=8	
	leaks all the time n=2	

*ICIQ-OAB - International Consultation on Incontinence Questionnaire Overactive Bladder;
ICIQ-LUTSQoL - International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Quality of Life;
ICIQ-UI SF- International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form

Neurological deficit measured by EDSS was found to positively correlate with LUTS on all three questionnaires: ICIQ-OAB (r=0.390, p<0.05), ICIQ-UI SF (r=0.477, p<0.01) and ICIQ-LUTSQoL (r=0.317, p<0.05) (Table 8).

25 patients were in treatment for depression. There were no significant differences between female and male patients regarding treatment for depression (χ^2=0.018, df=1, p>0.05) (Table 9). Results on ICIQ-UI SF on t-test show that depressive patients had more pronounced lower urinary tract symptoms when compared to non-depressive (t=2.067, df=99, p<0.05). This is also consistent with the results of the ICIQ-LUTSQoL (t=-2.193, df=99, p<0.05). There was no significant difference in results on ICIQ-OAB between depressive patients vs. non-depressive (t=-1.610, df=99, p>0.05) (Table 10). Positive correlations were found between depression and LUTS on ICIQ-UI SF (r=0.203, p<0.05) and ICIQ-LUTSQoL (r=0.215, p<0.05). Correlations were not found between depression and results on ICIQ-OAB (r=0.160, p>0.05) (Table 11).

Table 8. Neurological deficit measured by EDSS was found to positively correlate with LUTS on all three questionnaires: ICIQ-OAB (r=0.390, p<0.05), ICIQ-UI SF (r=0.477, p<0.01) and ICIQ-LUTSQoL (r=0.317, p<0.05)

		EDSS
EDSS	Pearson Correlation	1
	Sig. (2-tailed)	
	N	42
ICIQ-OAB_mean	Pearson Correlation	0.390*
	Sig. (2-tailed)	*0.011*
	N	42
ICIQ-UI SF_mean	Pearson Correlation	0.477**
	Sig. (2-tailed)	*0.001*
	N	42
ICIQ-LUTSQoL_mean	Pearson Correlation	0.317*
	Sig. (2-tailed)	*0.041*
	N	42

*EDSS - Expanded Disability Status Scale; ICIQ-UI SF - International Consultation on Incontinence Questionnaire-Urinary Incontinence; ICIQ-LUTSQoL - International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Quality of Life; ICIQ-OAB - International Consultation on Incontinence Questionnaire Overactive Bladder

Table 9. There were no significant differences between female and male patients regarding treatment for depression (χ^2=0.018, df=1, p>0.05) (Chi-Square Tests)

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	*0.018a*	*1*	*0.894*		
Continuity Correction[b]	0.000	1	1.000		
Likelihood Ratio	0.018	1	0.894		
Fisher's Exact Test				1.000	0.562
Linear-by-Linear Association	0.018	1	0.894		
N of Valid Cases	100				

[a] 0 cells (0.0%) have expected count less than 5. The minimum expected count is 6.25; [b] Computed only for a 2x2 table
χ^2 - Pearson Chi-Square

Table 10. Results on ICIQ-UI SF on t-test show that depressive patients had more pronounced lower urinary tract symptoms when compared to non-depressive (t=2.067, df=99, p<0.05). This is also consistent with results of the ICIQ-LUTSQoL (t=-2.193, df=99, p<0.05). There were no significant difference in results on ICIQ-OAB between depressive patients vs. non-depressive (t=-1.610, df=99, p>0.05)

		LTEV		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% CI Lower	95% CI Upper
ICIQ-UI SF_mean	EVA	3.468	0.066	-2.067	99	*0.041*	-1.06158	0.51366	-2.08078	-0.04237
	EVnA			-2.188	45.354	0.034	-1.06158	0.48527	-2.03875	-0.08440
ICIQ-OAB_mean	EVA	2.200	0.141	-1.610	99	0.111	-0.80708	0.50125	-1.80168	0.18752
	EVnA			-1.710	45.638	0.094	-0.80708	0.47201	-1.75739	0.14323
ICIQ-LUTSQoL_mean	EVA	1.285	0.260	-2.193	99	*0.031*	-0.62654	0.28567	-1.19336	-0.05971
	EVnA			-2.349	46.395	0.023	-0.62654	0.26672	-1.16330	-0.08977

LTEV - Levene's Test for Equality of Variances; 95% CI - 95% Confidence Interval of the Difference
EVA - Equal variances assumed; EVnA - Equal variances not assumed

*ICIQ-UI SF- International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form;
ICIQ-LUTSQoL - International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Quality of Life;
ICIQ-OAB - International Consultation on Incontinence Questionnaire Overactive Bladder

Table 11. Positive correlations were found between depression and LUTS on ICIQ-UI SF ($r=0.203$, $p<0.05$) and ICIQ-LUTSQoL ($r=0.215$, $p<0.05$). Correlations were not found between depression and results on ICIQ-OAB ($r=0.160$, $p>0.05$)

		Depression
Depression	Pearson Correlation	1
	Sig. (2-tailed)	
	N	101
ICIQ-OAB_mean	Pearson Correlation	0.160
	Sig. (2-tailed)	0.111
	N	101
ICIQ-UI SF_mean	Pearson Correlation	0.203*
	Sig. (2-tailed)	*0.041*
	N	101
ICIQ-LUTSQoL_mean	Pearson Correlation	0.215*
	Sig. (2-tailed)	*0.031*
	N	101

*EDSS - Expanded Disability Status Scale; ICIQ-UI SF - International Consultation on Incontinence Questionnaire-Urinary Incontinence; ICIQ-LUTSQoL - International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Quality of Life; ICIQ-OAB - International Consultation on Incontinence Questionnaire Overactive Bladder

DISCUSSION

Debilitating neurological disorders require a comprehensive, holistic, multidisciplinary approach throughout the entire disease to identify and minimise existing issues, maintain autonomy and improve patients' quality of life. MS is a progressive disease of the CNS, and it may be associated with severe disability necessitating palliative care approach (D'Amico et al. 2017).

Nearly 90% of patients with MS may experience some degree of voiding dysfunction and/or incontinence, and commonly report overactive bladder (OAB) symptoms of urinary urgency, incontinence and frequency, as well as the inability to void to completion. This may cause recurrent urinary tract infections, often leading to repeated hospitalizations and marked clinical decline (Aharony et al. 2017, Buljevac et al. 2002, Nikseresht et al. 2015, Tudor et al. 2016). The epidemiological data on the prevalence of LUTS in MS patients in Croatia is lacking. However, the results of this study show consistent results with other previously published literature on this topic worldwide. Health care professionals (HCPs) should be aware of potential LUTS in neurological patients. They should be adequately trained to recognise, identify, and treat them, as well as prevent long-term complications and consequently improve patients' quality of life. For this purpose questionnaires to help asses LUTS: ICIQ-OAB and ICIQ-LUTSQoL, were with permission successfully translated and validated into Croatian, while the questionnaire ICIQ-UI SF was already previously successfully validated for the Croatian language. These questionnaires were already used in the assessment of LUTS in patients with MS (Tudor et al. 2018) and were previously successfully validated for different languages (ICIQ). We hope that this will help promote the use of questionnaires among HCPs in Croatia in the evaluation of LUTS and help further improve the quality of management.

We found that a quarter of patients were in treatment for depression. Previous results relating to the prevalence of depression and anxiety in MS show some discrepancy, ranging from 14 to even 54%, and 1.24 to 36% (Hellmann-Regen et al. 2013, Liu & Tang 2018, Marrie et al. 2015, Zorzon et al. 2001). This study showed that the patients with depression had more pronounced LUTS, with positive correlations found between the two on ICIQ-UI SF and ICIQ-LUTSQoL. This, even more, highlights the need for a comprehensive approach regarding management and care of patients with MS. An earlier study by Ferreira et al. found the pelvic floor training program among women with MS resulted in improvement of QoL, OAB, perineal contraction, level of anxiety and depression (Ferreira et al. 2016). Aydin et al. found that foot reflexology as a part of OAB treatment helped relieve urinary and depressive symptoms with a positive effect on the QoL (Aydin et al. 2016). Results of the study by Di Rezze et al. suggest that duloxetine (an antidepressant acting as a selective serotonin-norepinephrine reuptake inhibitor) should be considered a first-choice drug in the treatment of MS patients presenting both depression and OAB and that it should also be considered as a suitable alternative or as concomitant treatment in MS patients with OAB but not experiencing depression (Di Rezze et al. 2012).

Limitations of this study include a small sample of patients. Also, there is a possibility that if further evaluation tools (e.g. questionnaires) were used to investigate the further presence of depressive symptoms in patients not treated for depression that the numbers would be higher. In the future, we intend to follow-up on our patients and hope to bring data on the bigger sample.

This study was performed with the idea of raising awareness and further clarification of bladder symptoms and depression in MS patients. Management should include appropriate assessment of both and therapy tailored accordingly.

CONCLUSION

This study gives insight into the presence of depression and LUTS in Croatian patients with MS for which purpose questionnaires to assess LUTS - ICIQ-OAB and ICIQ-LUTSQoL, were with permission successfully translated and validated into Croatian. The connection between depression and LUTS must be considered when managing patients with MS.

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Contribution of individual authors:

Katarina Ivana Tudor - conceived and designed the study, collected the data and contributed data or analysis tools, first draft, interpretation of the results, approval of the final version.

Marija Bošnjak Pašić - designed the study, collected the data and contributed data or analysis tools, interpretation of the results, approval of the final version.

Sandra Nađ Škegro, Mirko Bakula & Jakob Nemir - contributed data or analysis tools, literature searches and analyses.

Filip Mustač, Hanna Pašić & Luka Vujević - collected the data and contributed data or analysis tools.

Branka Vidrih & Lorainne Tudor Car - interpretation of the results, approval of the final version.

Fabijan Rajič - statistical analyses.

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