DOI: 10.4081/aiua.2022.1.46

ORIGINAL PAPER

Lower urinary tract symptoms and mental health during COVID-19 pandemic

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Summary *Objective: Coronaviruses (CoVs) are a group of RNA viruses involved in several human diseases affecting respiratory, enteric, hepatic, and neurological systems. COVID-19 was identified in 2020 and was named SARS-CoV-2. To limit worldwide contagion, many countries instituted a lockdown, which conducted to disruption of routine life. In fact, pandemic was associated with several stresses among population, such as loss of employment, deaths of family members, friends, or colleagues, financial insecurity, and isolation. This led to long-lasting psychosocial effects as anxiety and depression, increasing the prevalence of stress and trauma-related disorders in the population. The aim of this study was to investigate the correlation between lower urinary tracts symptoms (LUTS) and stress/depressive symptoms during COVID-19 pandemic.*

Materials and methods: An anonymous cross-sectional web-based survey (comprehending anthropometric data, education level, occupation status, smoking and alcohol habits, current therapies, quarantine and COVID-19 infection status) was conducted from March to May 2020 in Italy. LUTS were examined through National Institute of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) and Genitourinary Pain Index (GUPI). Hamilton Depression Rating Scale (HDRS) was utilized to evaluate depressive and anxiety symptoms. Non-parametric Kruskal-Wallis H Test was used for statistical analysis.

Results: A total of 356 out of 461 subjects fully completed the survey, with a response rate of 77.2%. Data showed that subjects involved in economic difficulties, quarantine measures or with increased HDRS reported a significative statistic worsened urinary symptoms ($H(3) = 11.731$, $p = 0.008$), quality of life, ($H(3) = 10.301$, $p = 0.016$), total NIH-CPSI/GUPI score ($H(3) = 42.150$, $p = 0.000$), and quality of life ($H(3) = 48.638$, $p = 0.000$).

Conclusions: COVID-19 pandemic provoked several alterations in everyday life. Although general lockdown, quarantine and social distancing have been necessary to prevent virus spreading, this had long term effects on all population in terms of mental and physical health. NIH-CPSI and GUPI scores increased linearly with stress and anxiety levels measured at HDRS, confirming worse LUTS in subjects who suffered anxiety and stress from COVID-19 pandemic.

KEY WORDS: *COVID-19; LUTS; NIH-CPSI; Anxiety; Stress; HDRS.*

Submitted 3 February 2022; Accepted 9 February 2022

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by a novel beta-coronavirus known as *Severe Acute Respiratory Syndrome Coronavirus 2* (SARS-CoV-2), firstly isolated in Wuhan, Hubei province of China (1-3). Since the first cases of SARS-Cov-2 reported in December 2019 in China, other Asian countries, such as Thailand, Japan and the Republic of Korea, reported increasing cases of COVID-19 in January 2020, leading the *World Health Organization* (WHO) to declare international public health emergency in the same month and, with the diffusion of contagion in Europe and North America, world pandemic in March 2020 (4). In order to limit the contagion, many countries instituted strict lockdown to flatten the epidemic curve and relieve the pressure on hospitals, permitting the activity only for essentials supply chains businesses and emergency/oncological healthcare services. The consequences related to social isolation, fear of infection and, particularly, the disruption of routine life, provoked severe detrimental and long-lasting psychosocial effects as anxiety and depression, increasing the prevalence of stress and trauma-related disorders in the population (5). Due to these premises and to the evidence that several urological conditions (as benign prostatic hyperplasia, overactive bladder, urge urinary incontinence, interstitial cystitis and bladder pain syndrome) were triggered or worsened after or during stressful events, the aim of our study was to explore how psychosocial consequences of COVID-19 affected lower urinary tract symptoms, considering in addition economic consequences and quarantine measures (6, 7).

MATERIALS AND METHODS

Study design

An anonymous cross-sectional, web-based closed survey between healthy subject was conducted, timed from March to May 2020, during lockdown period. The participants were recruited by an invitation distributed through direct e-mail and Facebook. Since its introduction in 2004, Facebook is the third most popular website in the world, with 1.65 billion monthly active users. Facebook is widely used among midlife and older adults,

No conflict of interest declared.

as well as reported by published studies with 63% of adults aged 50-64 and 56% of people 65 and older that use this platform. Several published studies reported this platform as a validated method of recruiting study participants for survey research (8, 9). The questionnaire was designed using the Google Form application included in the Google Drive office suite (Google LLC) and formulated in Italian, with the aim of increasing the response rate. The study was conducted according to the guidelines of the World Medical Association Declaration of Helsinki and to the current European GDPR privacy policy. Web-based survey was conducted according to the Checklist for Reporting Results of Internet E-Surveys (10). Subjects were informed at the beginning of the survey about purpose of the study, data storing and principal investigators (L.D and B.B). Data obtained were collected and stored on personal cloud of principal investigators, utilizing a two-step verification. Survey comprehended a first section with inclusion criteria, anthropometric data, education level, occupation status, smoking and alcohol habits, current therapies, quarantine and COVID-19 infection status. We defined as positive infection status, subjects with a diagnosis through nasopharyngeal swab at the time of the survey; suspicion infection status, subjects with clinical diagnosis (imaging or symptoms) in absence of nasopharyngeal swab at the time of the survey. Regarding quarantine status, we considered, in addition to the patients with diagnosed COVID-19 infection, subjects without COVID-19 infection but who had a close contact with a positive patient, according to the definition of *Center for Disease Control* and Prevention (CDC) (individual who has had closer than < 6 feet for ≥ 15 min with people with a positive diagnosis for COVID-19, whether symptomatic or asymptomatic). Inclusion criteria were: subjects over 18 years-old, without explainable urinary symptoms (urolithiasis, urinary infection, stress incontinence). Surveys not completely filled out were excluded by further analysis. Second section of the survey comprehended *National Institute of Health-Chronic Prostatitis Symptom Index* (NIH-CPSI) for males and *Genitourinary Pain Index* (GUPI) for females (11, 12). Third section of the survey comprehended, finally, *Hamilton Depression Rating Scale* (HDRS) (13). Survey was tested by all investigators in order to verify usability and technical functionality. Successively, survey was submitted, through Google Forms, to the most used social networks.

Statistical analysis

Descriptive statistics included means and standard deviations for continuous variables while frequencies and percentages were obtained for categorical variables. Non-parametric Kruskal-Wallis H Test was used to determine differences between groups, according to normality assumptions examined with Kolmogorov-Smirnov Test, and was performed on NIH-CPSI/GUPI subscales (pain, urinary symptoms, quality of life) and total results, stratifying the analysis for: COVID-19 infection status, economic consequences, quarantine measures, and HDRS total score. Finally, Kruskal-Wallis H Test was performed to compare HDRS score grading (0-7: no depression; 8-17: mild depression; 18-24: moderate depression; > 24: severe depression) to NIH-CPSI/GUPI parameters.

All statistical analyses were performed using *International Business Machines Corporation Statistical Product and Service Solutions* (IBM SPSS) software for Windows (*version 25.0., IBM Corp, Armonk, NY, USA*). Statistical significance was defined as $p < 0.05$.

Results

A total of 356 out of 461 subjects fully completed the survey, for a completion rate of 77.2%. Descriptive statistics obtained are reported in Table 1.

COVID-19 Infection status

We compared the results of NIH-CPSI/GUPI and HDRS in subjects with diagnosed (n = 4), negative (n = 329) and suspected (n = 23) COVID-19 infection. COVID-19 infection status reported statistically significant differences for pain ($H(2) = 6.825$, $p = 0.033$) and quality of life ($H(2) = 6.187$, $p = 0.045$) subscales, while no statistically significant differences were reported for urinary symptoms subscale ($H(2) = 0.716$, $p = 0.699$), total score ($H(2) = 5.667$, $p = 0.059$) and HDRS score ($H(2) = 3.491$, $p = 0.175$). In particular, negative infection status subjects reported in pain subscale a mean rank of 178.64

Table 1.
Descriptive statistics of subjects involved.

	Mean	Standard deviation
Age	36.49	12.236
Height (in m)	1.70	0.08
Weight	72.28	17.11
BMI	24.77	4.65
	Frequency	**Percentage**
Sex		
Male	182	51.1
Female	174	48.9
Marital status		
Single	201	56.5
Married/in a couple	135	37.9
Divorced	16	4.5
Widow/widower	4	1.1
Education level		
Low	10	2.8
Medium	110	30.9
High	236	66.3
Working status		
Employed	237	66.6
Unemployed	119	33.4
COVID-19 infection status		
Negative	329	92.4
Suspicion	23	6.5
Positive	4	1.1
Economic consequences		
Financial hardship	113	31.3
Job loss	13	3.6
Quarantined	68	19.1
Diabetes	10	2.8
Hypertension	30	8.4
Obese	20	5.6
Depression	7	2
Asthma	34	9.6
COPD	3	0.8
Cardiovascular disease	10	2.8
Alcohol	76	21.3
Smoking	103	28.9

while suspicious infection status subjects reported a mean rank of 158.65 and, finally, positive infection status subjects reported a mean rank of 281.13. Analogously, negative infection status subjects reported in quality-of-life subscale a mean rank of 179.97 compared to suspicious infection status subjects (mean rank of 143) and positive infection status subjects (mean rank of 261.88).

Economic consequences

We compared the results of NIH-CPSI/GUPI and HDRS in subjects who suffered financial hardship (n = 113) or job loss (n = 13) compared to no economic consequences (n = 230). Economic consequences were classified as none, financial hardship, or job loss. Statistically significant differences were reported for urinary symptoms (H(3) = 11.731, p = 0.008), quality of life (H(3) = 10.301, p = 0.016), total score (H(3) = 14.537, p = 0.002) and HDRS score (H(3) = 20.706, p = 0.000), while no statistically significant difference was reported for pain subscale (H(3) = 6.242, p = 0.100). Mean ranks for urinary symptoms were 165.27 for no economic consequences, 204.9 for financial hardship and 175.46 for job loss. Mean ranks for quality of life were, similarly: 167.68 (no consequences), 193.12 (financial hardship) and 237.85 (job loss). Mean ranks for total score were 163.01 (no consequences), 205.54 (financial hardship), and 212.69 (job loss). Finally, mean rank for HDRS score were 158.88 (no consequences), 209.19 (financial hardship), and 226.35 (job loss).

Quarantine measures

We compared the results of NIH-CPSI/GUPI and HDRS in subjects who underwent to quarantine measures (n = 68) compared to who had no restrictions (n = 288). HDRS score was statistically significant different between subjects who underwent to quarantine measures (e.g: direct contact with infected patients) and not (H(1) = 7.179, p = 0.007), reporting a mean rank of 208.53 for subjects in quarantine *versus* 171.41 for those who underwent no measures. No statistically significant differences were instead reported for pain (H(1) = 3.130, p = 0.077), urinary symptoms (H(1) = 0.596, p = 0.440) and quality of life subscales (H(1) = 2.616, p = 0.106). Similarly, no statistically significant difference was reported for NIH-CPSI/GUPI total score (H(1) = 2.088, p = 0.148)

HDRS score grading

According to HDRS score grading, we divided subjects in four groups: no depression (n = 187), mild depression (n = 133), moderate depression (n= 26) and severe depression (n = 10). We further correlated HDRS score grading with NIH-CPSI/GUPI results, reporting statistically significant differences for pain (H(3) = 40.093, p = 0.000), urinary symptoms (H(3) = 42.150, p = 0.000), quality of life (H(3) = 48.638, p = 0.000) and total score (H(3) = 66.480, p = 0.000). In particular, mean ranks for pain were 155.02 for no depression, 195.76 for mild depression, 217.10 for moderate depression and 287.70 for severe depression. Similarly, mean ranks for urinary symptoms were 147.97 (no depression), 203.04 (mild depression), 245.33 (moderate depression) and 249.40 (severe depression). Mean ranks for quality of life were similarly: 148.84 (no depression), 198.70 (mild depression), 249.77 (moderate depression) and 279.10 (severe depression). Finally, mean ranks for total score were 140.25 (no depression), 208.18 (mild depression), 254.56 (moderate depression) and 301.35 (severe depression).

Discussion

The COVID-19 pandemic has embodied several stresses such as loss of employment, deaths of family members, friends, or colleagues, financial insecurity, and isolation from others (14). The social isolation, the fear of contagion and the imposed limitations, have created a fertile substrate for anxiety and post-traumatic stress disorders development (15). In addition, the impossibilities to work, socialize with others and to engage in physical activities produced increased distress levels and contributed to overall decline in health, further aggravating the psychobiological impact of the outbreak (16).

Stressful events could alter body homeostasis, triggering and/or aggravating several pathologies and diseases (17). However, if this relation is well-known and demonstrated for gastrointestinal, dermatologic and cardiovascular diseases, interactions between elevated stress levels and urological conditions remain controversial (18). In the urological field, COVID-19 pandemic has increased sexual disturbances, as reported by the decreased erectile function and increased premature ejaculation incidence in men, together with a decreased PDE5i interest (as reported on Google trend analysis) (19, 20). Regarding urinary disturbances, animal models have indeed shown how social stress could impair bladder function, up to developing a proper generalised bladder mucosal inflammation (21). A study by *Ullrich et al.* showed on men with BPH a worsening of symptoms when subjects were exposed to standardized laboratory stress tasks (22). Similarly in women, the prevalence of overactive bladder and other LUTS were increased among subjects with increased occupational stress (23). *Lower urinary tract symptoms* (LUTS) conversely, have been associated with acute and chronic stress, and with other stress-related pathologies, such as gastroenterological complaints, irritable bowel syndrome, vulvodynia, dyspareunia and even odontostomatological conditions (24, 25).

Due to these premises, we evaluated the relationship between stressful events, as COVID-19 worldwide pandemic, and urological manifestations, excluding subjects with explainable causes for LUTS. Furthermore, we analysed how mental health correlated with LUTS. In addition, although we reported in our cohort of subjects different comorbidities which could have impacted the results of our survey, none of them reached the statistical significance at the statistical analysis.

Regarding COVID-19 infection status, we reported increased NIH-CPSI/GUPI score for pain and quality of life subscales in subjects with active or suspicion infection. Although we suggest that these results were associated more with the stressful event itself rather than a direct interaction of coronavirus, our data is consistent with recent hypotheses reported in literature. *Dhar et al.* indeed, reported 39 COVID-19 patients who developed

de novo urinary symptoms while *Kaya et al.* similarly, reported 46 COVID-19 patients with increased storage symptoms during hospitalization (26, 27). However, due to the limited number of subjects diagnosed with COVID-19 infection in our study, the results obtained are obviously weakened and limited.

When economic consequences of lockdown and worldwide pandemic were analysed, we reported increased score in urinary symptoms and quality of life subscales together with an increased overall NIH-CPSI/GUPI score. HDRS score was increased as well. Although the definition of financial hardship is quite subjective, job and financial insecurity have serious consequences on physical and mental health of individuals (28). Among several adverse health outcomes, increased psychosomatic symptoms as anxiety and depression are reported(29). The presence of increased HDRS score for subjects with financial hardship or job loss was indeed perfectly consistent with data reported in literature. Similarly, subjects which suffered financial hardship or job loss during lockdown reported increased urinary symptoms and a worsened quality of life. Also in this case, we suggest that the increased psychological burden linked to the difficult socioeconomical situation influenced symptoms manifestations (30). Similarly, when quarantine measures were considered, HDRS score increased in subjects quarantined. As reported by *Giallonardo et al.*, social distancing and quarantine have detrimental effects on mental health, both in general population and in psychiatric patients, thus confirming the consistence of our data (31). No significant differences in NIH-CPSI/GUPI score however were reported.

Finally, we correlated HDRS score with NIH-CPSI/GUPI score. We reported significant differences for every subscale and total score. As far as we know, there is only a study correlating HDRS score and LUTS: *Skalski et al.* used HDRS and IPSS score on 102 patients treated for depression, reporting a significant correlation between severity of depressive symptoms and severity of LUTS (32). Our study confirms this correlation, showing increasing NIH-CPSI/GUPI score with increasing results of HDRS score. We are conscious of several limitation of our study: firstly, the retrospective and self-reported nature or our study; secondly, a relatively low sample size for exploring interactions between COVID-19 infection or quarantine measures and LUTS; thirdly, the geographical limitation of our results; fourthly, an overall low mean age which could represent the decreased and heterogeneous use of internet-based instruments of older subjects, potentially excluding them from our study (33). Finally, the restricted number of properly diagnosed COVID-19 patients limits the reliability of our results regarding COVID-19 and urinary symptoms.

Conclusions

COVID-19 pandemic has provoked notable alterations in everyday life. Although general lockdown, quarantine and social distancing have been necessary in order to prevent virus spreading, detrimental effects of strict lockdown could have long term effects on population in terms of mental and physical health. The association between stressful events and increased LUTS has been explored during lockdown in southern Italy, confirming a preponderant role of stress and anxiety in LUTS development and suggesting a bidirectional relationship between mental health and urological symptoms. Further studies are required to fully evaluate this relationship and explore the direct effect of SARS-CoV-2 on LUTS.

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