



Urological complications after COVID 19 vaccine according to age, sex and manufacturer

Sung Ryul Shim^{1,2} · Kwang Taek Kim⁴ · Eunju Park^{2,3} · Jong Hyun Pyun⁵ · Jae Heon Kim⁶ · Benjamin I. Chung⁷

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Abstract

Objectives To examine the effects of age, sex, and type of COVID-19 vaccine on urological complications after vaccination with COVID-19.

Materials and methods We used the Vaccine Adverse Event Reporting System (VAERS) data from December 2020 to August 2022 to analyze urological symptoms post-vaccination adverse events (AEs) associated with COVID-19 vaccines authorized for the U.S. population. We collected AEs after 1–2 dose vaccination in VAERS, but not those after an additional booster shot. Age was divided into three groups (< 18 years, 18–64 years, and > 64 years), and compared incidence of AEs after vaccination with either mRNA vaccine (mRNA-1273, Moderna; and BNT162b2, Pfizer-BioNTech) or a viral vector vaccine (JNJ-78436735, Janssen/Johnson and Johnson) as reported in VAERS data.

Results Cumulative incidence rates (CIRs) of LUTS, voiding symptom, storage symptom, infection, and hematuria were 0.057, 0.282, 0.223, 1.245, and 0.214, respectively. By gender, CIRs OF LUTS, storage symptom, and infection were statistically significantly higher in women, whereas CIRs of voiding symptom and hematuria were statistically significantly higher in men. CIRs of AEs per 100,000 in age groups of < 18 years, 18–64 years, and > 64 years were 0.353, 1.403, and 4.067, respectively. All AE types except for voiding symptom displayed the highest CIRs in the Moderna vaccine group.

Conclusions Based on an updated analysis of available data, the prevalence of urologic complications following administration of COVID-19 vaccines is low. However, specific urologic complications such as gross hematuria are not low in incidence.

Keywords COVID-19 · Vaccination · Urologic symptoms · Urologic side effects

Introduction

Patients who suffer from urological conditions and their health care providers have been profoundly affected by the COVID-19 pandemic [1]. The world has seen a vast increase in the incidence and mortality rates caused by the SARS-CoV-2 virus. These are changing from day to day [2]. As of

Sung Ryul Shim & Kwang Taek Kim contributed equally to this work as co-first authors. Jong Hyun Pyun & Jae Heon Kim contributed equally to this work as co-corresponding authors.

✉ Jong Hyun Pyun
docpjh79@hanmail.net

✉ Jae Heon Kim
piacekjh@hanmail.net

¹ Department of Biomedical Informatics, College of Medicine, Konyang University, 158 Gwanjeodong-ro, Seo-gu, Daejeon 35365, Republic of Korea

² Evidence Based Research Center, Kyungnam University, Changwon, Republic of Korea

³ Department of Food and Nutrition, Kyungnam University College of Health Sciences, Changwon, Republic of Korea

⁴ Department of Urology, Gil Medical Center, Gachon University College of Medicine, Incheon, Republic of Korea

⁵ Department of Urology, Kangbuk Samsung Hospital, Kangbuk Samsung Medical Center, Sungkyunkwan University School of Medicine, 29 Saemunan-ro, Jongno-gu, Seoul 03181, Korea

⁶ Department of Urology, Soonchunhyang University Hospital, Soonchunhyang University College of Medicine, 59 Daesagwan-ro, Yongsan-gu, Seoul 04401, Republic of Korea

⁷ Department of Urology, Stanford University Medical Center, Stanford, CA, USA

November 28, 2022, the World Health Organization (WHO) reported that a total of 636,440,663 people have contracted the disease of which 6,606,624 have died [3]. With the absence of a specific therapy for COVID-19, vaccination has been identified as a major strategy to fight the rapid spread of this virus. Vaccines produced by several pharmaceutical companies such as AstraZeneca, Janssen, Pfizer/BioNTech, and Moderna have been granted emergency use authorization by the United States Food and Drug Administration (FDA) in effort to curb the spread of the COVID-19 pandemic. These vaccines work by eliciting antibodies to provide immunity against SARS-CoV-2 infection [4]. COVID-19 vaccines provided by both Pfizer/BioNTech and Moderna are mRNA vaccines while those provided by AstraZeneca and Janssen are adenovirus vaccines.

Although these vaccines have hardly been approved for a year, they are already rolled out for administration to the wider public. The Pfizer-BioNTech COVID-19 vaccine and the Moderna COVID-19 vaccine were granted Emergency Use Authorization by the US FDA on December 11, 2020 and December 18, 2020, respectively [5]. By February 12, 2021, more than 54 million doses have been given to US residents [6]. Among all other vaccines approved in the past, only vaccine for mumps was developed and approved this fast way back in the 1960s, which took a total of 4 years from viral sampling to approval [7].

Several countries have developed their own reporting and monitoring systems to keep track of common as well as serious adverse events following a vaccination program. Although many of these events are carefully recorded and monitored, data regarding organ specific complications related to vaccine administration are scarce [1, 8]. Zhao et al. [9] have reported that urologic symptoms following a COVID-19 vaccination are extremely rare. However, recent studies have shown the emergence of urologic complications including gross hematuria after a COVID-19 vaccination [10–12].

Using the largest data set from the Vaccine Adverse Event Reporting System (VAERS) and data from the Centers for Disease Control and Prevention (CDC) COVID 19 Vaccination in the US, we examined the incidence of urologic complications after a COVID-19 vaccination in this study. Effects of age, sex, and the type of COVID-19 vaccine administered on the resulting urologic complications were also analyzed.

Methods

This study followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines (Supplementary Table 2).

Database description

We used VAERS data from December 2020 to August 2022 to analyze urological symptoms post-vaccination adverse events (AEs) associated with COVID-19 vaccines authorized for the U.S. population. The VAERS was developed in 1990 as a US vaccine safety surveillance program by the CDC and the FDA. It collects information regarding AEs to serve as an early warning system for potential safety issues with US-licensed vaccines. Vaccine recipients, health care providers, and vaccine makers can openly report side effects to the VAERS [13].

Adverse event and study population

Urological AEs were based on Medical Dictionary for Regulatory Activities (MedDRA) concepts at the preferred term (PT) level [14], and considered PTs are shown in supplementary files 1. Two investigators (S.R. Shim and J.H. Kim) independently screened descriptions in the database to ensure the reliability of urological diagnosis of AEs. They also examined all narrative texts of coexisting current illnesses and comorbidities in VAERS.

Setting and study population

Since VAERS does not provide information for the entire vaccination population, we assumed that the total population in CDC Data Tracker were people who had received the second dose in a two-dose COVID-19 vaccine primary series or one dose of a single-dose COVID-19 vaccine primary series approved or authorized for use in the United States. Therefore, we collected AEs after 1–2 dose vaccination in VAERS, but not those after an additional booster shot.

Age was divided into three groups (< 18 years, 18–64 years, and > 64 years) and we compared incidence of AEs after vaccination with either mRNA vaccine (mRNA-1273, Moderna; and BNT162b2, Pfizer-BioNTech) or a viral vector vaccine (JNJ-78436735, Janssen/Johnson and Johnson) as reported in VAERS data.

Statistical analysis

Cumulative incidence rates (CIRs) of AEs per 100,000 for people fully vaccinated with COVID-19 vaccine in the US were calculated for each specific symptom. We then illustrated CIRs by sex, age, and manufactures. Pearson's χ^2 -test or Fisher's exact test was carried out to determine statistically significant differences between categories. All statistics were two-tailed and p values < 0.05 were considered to be significant. R

version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria) was used for all statistical analyses.

Results

The initial search identified a total 4485 of urological AEs from the VAERS database. The number of fully vaccinated people was 221,950,982 in US from the CDC Data Tracker. Numbers of AEs in Pfizer-BioNTech, Moderna, and Janssen vaccine groups were 2176 (48.0%), 2063 (45.5%), and 294 (6.5%), respectively. Numbers of fully vaccinated people in Pfizer-BioNTech, Moderna, and Janssen vaccine groups were 128,558,022 (57.6%), 77,647,511 (34.8%), and 17,064,965 (7.6%), respectively.

Flow diagram of this study and CIRs of AE types per 100,000 for people fully vaccinated with COVID-19 vaccine are presented in supplementary Fig. 1 and 2. Overall CIR of total AEs was 2.021. CIRs of Lower Urinary Tract Symptom (LUTS), voiding symptom, storage symptom, infection, and hematuria were 0.057, 0.282, 0.223, 1.245, and 0.214, respectively. By gender, CIRs of LUTS, storage symptom, and infection were statistically significantly higher in women, whereas CIRs of voiding symptom and hematuria were statistically significantly higher in men. Among individual symptoms, frequencies of urinary tract infection, hematuria, and pelvic pain were the highest at 1,952, 426, and 422 (Table 1).

Among age groups, with an increasing in age, CIRs of all AEs were also significantly increased. CIRs of AEs per 100,000 in age groups of < 18 years, 18–64 years, and > 64 years were 0.353, 1.403, and 4.067, respectively. Urinary tract infections showed the highest CIR at 2.135 in the age group of > 64 years (Table 2).

By vaccine manufacturer, CIRs of AE per 100,000 in Pfizer-BioNTech, Moderna, and Janssen vaccine groups were 1.693, 2.657, and 1.723, respectively. All AE types except for voiding symptom displayed the highest CIRs in the Moderna vaccine group. CIRs of urine abnormality, urinary retention, micturition urgency, bladder discomfort, bladder pain, cystitis, and hematuria in the Moderna vaccine group were statistically higher than those in other vaccine groups. CIRs of lower urinary tract symptoms, benign prostatic hyperplasia, and nocturia in Janssen vaccine group were statistically higher than those in other vaccine groups. Pfizer-BioNTech showed relatively low CIRs (Table 3).

Discussion

Our investigation found that only a few studies so far had examined urologic complications following a COVID-19 vaccination [15, 16]. We also found that no study had compared the prevalence of urologic complications according

to the type of COVID-19 vaccine (vector vaccine or mRNA vaccine) administered.

In this study, we examined the prevalence of urologic complications based on age, sex, and the type of COVID-19 vaccine administered in detail.

It is known that an increase in age is linked to a reduction in vaccine effectiveness [17]. The study conducted by Ritter et al. [12] showed the incidence of certain side effects such as acute kidney injury. However, their study did not show other urologic complications such as lower urinary tract infections or hematuria.

Our study showed that as age increased, all CIRs of AEs also increased significantly. CIR of AEs per 100,000 was 0.353 for those under 18 years of age, 1.403 for those aged 18–64 years, and 4.067 for those aged over 64 years. Urinary tract infections showed the highest CIR of 2.135 in the age group of over 64 years.

Although it has been reported that the prevalence of vaccine complications is higher in women than in men, this finding still needs more exhaustive research. These are largely affected by interactions between environmental factors and sex hormones [18]. A prospective study conducted by Giurgea et al. [19] has demonstrated sex differences in influenza infection based on data collected from 164 healthy volunteers undergoing influenza A/California/04/2009/H1N1 challenge to show differences in immune responses between sexes. It showed that women and their cohorts were more likely to be symptomatic with a higher number of symptoms than men. This indicates that while women might actually have more side effects and report them more often than men, they might also benefit more from protective properties of a vaccine.

Potluri et al. [20] have shown that the benefit of an elevated estradiol in antibody responses and protection against influenza decreases with age in both mice and humans. The present study showed differences in symptoms between sexes. For instance, CIRs of LUTS, storage symptoms, and infections were significantly higher in women whereas CIRs of voiding symptom and hematuria were significantly higher in men.

When it comes to post-vaccination AEs, many recent studies based on self-reported side effects by health sector workers from both mRNA-based (Moderna and Pfizer-BioNTech) and viral vector-based (AstraZeneca) vaccines have demonstrated the occurrence of a broad spectrum of symptoms. These symptoms ranged from the most common symptoms such as localized pain around the injection site or a sore arm to more generalized symptoms of weakness or fatigue [21–25]. Three studies have reported the occurrence of urological AEs, the most common urological AE was urinary urgency with an occurrence rate of 0.75% after a COVID-19 BNT162b2 mRNA vaccine and 1.16% after a COVID-19 mRNA-1273 vaccine [22, 23]. The second most

Table 1 Urological adverse events by COVID-19 vaccinations by sex in the United States

Symptoms	Sum		Male		Female		<i>P</i> value*
	Frequency	CIR	Frequency	CIR	Frequency	CIR	
LUTS	126	0.057	41	0.039	85	0.073	0.001
Lower urinary tract symptoms	17	0.008	8	0.008	9	0.008	0.963
Urine abnormality	109	0.049	33	0.031	76	0.065	0.000
Voiding symptom	626	0.282	348	0.329	278	0.239	0.000
Benign prostatic hyperplasia	51	0.023	50	0.047	1	0.001	0.000
Urinary hesitation	18	0.008	10	0.009	8	0.007	0.500
Urinary straining	2	0.001	1	0.001	1	0.001	1.000
Urethral obstruction	4	0.002	4	0.004	–	0.000	0.051
Urinary tract obstruction	12	0.005	9	0.009	3	0.003	0.058
Bladder obstruction	1	0.000	1	0.001	–	0.000	0.476
Bladder outlet obstruction	2	0.001	2	0.002	–	0.000	0.227
Bladder neck obstruction	1	0.000	1	0.001	–	0.000	0.476
Urinary retention	280	0.126	147	0.139	133	0.114	0.102
Urine flow decreased	19	0.009	9	0.009	10	0.009	0.983
Urine output	32	0.014	18	0.017	14	0.012	0.328
Urine output decreased	169	0.076	86	0.081	83	0.071	0.395
Urine output increased	33	0.015	10	0.009	23	0.020	0.046
Urethral atrophy	2	0.001	–	0.000	2	0.002	0.501
Storage symptom	494	0.223	125	0.118	369	0.317	0.000
Urge incontinence	3	0.001	1	0.001	2	0.002	1.000
Urinary bladder suspension	1	0.000	–	0.000	1	0.001	1.000
Hypertonic bladder	21	0.009	4	0.004	17	0.015	0.009
Micturition urgency	245	0.110	56	0.053	189	0.163	0.000
Nocturia	38	0.017	19	0.018	19	0.016	0.769
Bladder dilatation	17	0.008	10	0.009	7	0.006	0.355
Bladder discomfort	30	0.014	6	0.006	24	0.021	0.002
Bladder disorder	76	0.034	18	0.017	58	0.050	0.000
Bladder dysfunction	27	0.012	7	0.007	20	0.017	0.024
Bladder irritation	6	0.003	–	0.000	6	0.005	0.032
Bladder spasm	29	0.013	3	0.003	26	0.022	0.000
Bladder stenosis	1	0.000	1	0.001	–	0.000	0.476
Infection	2,764	1.245	609	0.576	2,155	1.854	0.000
Urinary tract infection	1,952	0.879	473	0.448	1,479	1.272	0.000
Bladder pain	96	0.043	13	0.012	83	0.071	0.000
Cystitis	268	0.121	55	0.052	213	0.183	0.000
Prostatitis	21	0.009	21	0.020	–	0.000	0.000
Pelvic pain	422	0.190	44	0.042	378	0.325	0.000
Urethritis	5	0.002	3	0.003	2	0.002	0.674
Hematuria	475	0.214	268	0.254	207	0.178	0.000
Hematuria	426	0.192	244	0.231	182	0.157	0.000
Urinary bladder hemorrhage	13	0.006	8	0.008	5	0.004	0.315
Urinary occult blood	1	0.000	–	0.000	1	0.001	1.000
Urinary occult blood negative	20	0.009	5	0.005	15	0.013	0.043
Urinary occult blood positive	15	0.007	11	0.010	4	0.003	0.046
Overall CIR	4,485	2.021	1,391	1.316	3,094	2.661	0.000
People fully vaccinated of COVID-19 vaccinations in the US	221,950,982		105,691,883		116,259,099		

CIR cumulative Incidence rate per 100,000 by people fully vaccinated of COVID-19 vaccinations in the US

*Statistically significant differences between male and female categories using χ^2 test or Fisher's exact test

Table 2 Urological adverse events of COVID-19 vaccination by age in the United States

Symptoms	< 18		18–64		> 64		P value*
	Frequency	CIR	Frequency	CIR	Frequency	CIR	
LUTS	4	0.017	77	0.052	42	0.083	0.001
Lower urinary tract symptoms	1	0.004	10	0.007	6	0.012	0.491
Urine abnormality	3	0.012	67	0.045	36	0.071	0.002
Voiding symptom	16	0.066	282	0.189	311	0.618	0.000
Benign prostatic hyperplasia	–	0.000	4	0.003	46	0.091	0.000
Urinary hesitation	–	0.000	13	0.009	5	0.010	0.359
Urinary straining	–	0.000	1	0.001	1	0.002	0.574
Urethral obstruction	–	0.000	3	0.002	1	0.002	1.000
Urinary tract obstruction	–	0.000	1	0.001	8	0.016	0.001
Bladder obstruction	–	0.000	1	0.001	–	0.000	1.000
Bladder outlet obstruction	–	0.000	–	0.000	2	0.004	0.103
Bladder neck obstruction	–	0.000	–	0.000	1	0.002	0.339
Urinary retention	6	0.025	138	0.093	133	0.264	0.000
Urine flow decreased	1	0.004	12	0.008	5	0.010	0.820
Urineoutput	3	0.012	11	0.007	14	0.028	0.005
Urine output decreased	4	0.008	75	0.050	87	0.173	0.000
Urine output increased	–	0.017	21	0.014	8	0.016	0.884
Urethral atrophy	–	0.000	2	0.001	–	0.000	1.000
Storage symptom	3	0.012	308	0.207	163	0.324	0.000
Urge incontinence	–	0.000	1	0.001	1	0.002	0.550
Urinary bladder suspension	–	0.000	1	0.001	–	0.000	1.000
Hypertonic bladder	–	0.000	14	0.009	7	0.014	0.185
Micturition urgency	2	0.008	163	0.109	73	0.145	0.000
Nocturia	1	0.004	17	0.011	16	0.032	0.005
Bladder dilatation	–	0.000	5	0.003	12	0.024	0.001
Bladder discomfort	–	0.000	22	0.015	7	0.014	0.153
Bladder disorder	–	0.000	47	0.032	21	0.042	0.009
Bladder dysfunction	–	0.000	13	0.009	14	0.028	0.004
Bladder irritation	–	0.000	1	0.001	5	0.010	0.008
Bladder spasm	–	0.000	23	0.015	7	0.014	0.141
Bladder stenosis	–	0.000	1	0.001	–	0.000	1.000
Infection	26	0.108	1,225	0.822	1,309	2.599	0.000
Urinary tract infection	17	0.071	704	0.473	1,075	2.135	0.000
Bladder pain	1	0.004	70	0.047	22	0.044	0.010
Cystitis	2	0.008	100	0.067	140	0.278	0.000
Prostatitis	–	0.000	14	0.009	6	0.012	0.248
Pelvic pain	6	0.025	334	0.224	64	0.127	0.000
Urethritis	–	0.000	3	0.002	2	0.004	0.774
Hematuria	36	0.150	198	0.133	223	0.443	0.000
Hematuria	34	0.141	189	0.127	185	0.367	0.000
Urinary bladder hemorrhage	–	0.000	3	0.002	10	0.020	0.001
Urinary occult blood	1	0.004	–	0.000	–	0.000	0.108
Urinary occult blood negative	–	0.000	3	0.002	17	0.034	0.001
Urinary occult blood positive	1	0.004	3	0.002	11	0.022	0.001
Overall CIR	85	0.353	2,090	1.403	2,048	4.067	0.000
People fully vaccinated of COVID-19 vaccinations in the US	24,075,890		148,941,175		50,357,418		

CIR cumulative incidence rate per 100,000 by people fully vaccinated of COVID-19 vaccinations in the US

*Statistically significant differences between male and female categories using χ^2 test or Fisher's exact test

Table 3 Urological adverse events of COVID-19 vaccination by manufacturer in the United States

Symptoms	PFIZER.BIONTECH		MODERNA		JANSSEN		<i>P</i> value*
	Frequency	CIR	Frequency	CIR	Frequency	CIR	
LUTS	59	0.046	60	0.077	10	0.059	0.016
Lower urinary tract symptoms	11	0.009	4	0.005	2	0.012	0.441
Urine abnormality	48	0.037	56	0.072	8	0.047	0.003
Voiding symptom	285	0.222	285	0.367	63	0.369	0.000
Benign prostatic hyperplasia	22	0.017	17	0.022	11	0.064	0.002
Urinary hesitation	10	0.008	7	0.009	1	0.006	0.925
Urinary straining	–	0.000	1	0.001	1	0.006	0.064
Urethral obstruction	2	0.002	2	0.003	–	0.000	0.732
Urinary tract obstruction	4	0.003	6	0.008	2	0.012	0.144
Bladder obstruction	1	0.001	–	0.000	–	0.000	1.000
Bladder outlet obstruction	–	0.000	2	0.003	–	0.000	0.267
Bladder neck obstruction	1	0.001	–	0.000	–	0.000	1.000
Urinary retention	122	0.095	134	0.173	28	0.164	0.000
Urine flow decreased	9	0.007	8	0.010	2	0.012	0.491
Urine output	16	0.012	17	0.022	1	0.006	0.188
Urine output decreased	83	0.065	73	0.094	14	0.082	0.061
Urine output increased	15	0.012	16	0.021	3	0.018	0.240
Urethral atrophy	–	0.000	2	0.003	–	0.000	0.251
Storage symptom	247	0.192	217	0.279	34	0.199	0.000
Urge incontinence	1	0.001	1	0.001	1	0.006	0.254
Urinary bladder suspension	1	0.001	–	0.000	–	0.000	1.000
Hypertonic bladder	13	0.010	8	0.010	1	0.006	1.000
Micturition urgency	120	0.093	113	0.146	15	0.088	0.002
Nocturia	12	0.009	20	0.026	5	0.029	0.003
Bladder dilatation	6	0.005	11	0.014	–	0.000	0.043
Bladder discomfort	12	0.009	17	0.022	1	0.006	0.051
Bladder disorder	50	0.039	21	0.027	5	0.029	0.347
Bladder dysfunction	14	0.011	12	0.015	1	0.006	0.571
Bladder irritation	4	0.003	2	0.003	–	0.000	1.000
Bladder spasm	14	0.011	12	0.015	4	0.023	0.304
Bladder stenosis	–	0.000	–	0.000	1	0.006	0.078
Infection	1,331	1.035	1,300	1.674	158	0.926	0.000
Urinary tract infection	895	0.696	965	1.243	113	0.662	0.000
Bladder pain	46	0.036	47	0.061	3	0.018	0.008
Cystitis	150	0.117	114	0.147	8	0.047	0.002
Prostatitis	8	0.006	10	0.013	3	0.018	0.126
Pelvic pain	231	0.180	161	0.207	30	0.176	0.345
Urethritis	1	0.001	3	0.004	1	0.006	0.106
Hematuria	254	0.198	201	0.259	29	0.170	0.006
Hematuria	222	0.173	187	0.241	26	0.152	0.001
Urinary bladder hemorrhage	6	0.005	4	0.005	3	0.018	0.128
Urinary occult blood	1	0.001	–	0.000	–	0.000	1.000
Urinary occult blood negative	14	0.011	6	0.008	–	0.000	0.511
Urinary occult blood positive	11	0.009	4	0.005	–	0.000	0.509
Overall CIR	2,176	1.693	2,063	2.657	294	1.723	0.000
People fully vaccinated of COVID-19 Vaccinations in the US	128,558,022		77,647,511		17,064,965		

CIR cumulative incidence rate per 100,000 by people fully vaccinated of COVID-19 vaccinations in the US

*Statistically significant differences between male and female categories using χ^2 test or Fisher's exact test

common reported urological AE was urinary frequency at a rate of 0.37% after administration of a BNT162b2 mRNA vaccine and 0.69% after administration of an mRNA-1273 vaccine. The present study showed that infection was the most common complication after a COVID-19 vaccination. It was largely noticeable among women. The second most common complication we found was voiding symptoms.

More recent studies have highlighted the clinical importance of gross hematuria after a COVID-19 vaccination [10–12, 16]. It has been reported lately that the presence of gross hematuria after vaccination is a diagnosed IgA nephropathy and that gross hematuria that occurs after vaccination in patients with nephropathy is a clinical symptom of acute respiratory failure [10–12, 16]. Moreover, although there have been no reported cases of vaccine related cancer side effect, gross hematuria is considered an important clinical symptom of tumors occurring in the kidneys, ureters, bladder, and urethra in addition to nephropathy [26]. The present study showed the overall CIR of hematuria was 0.183, which was more prevalent in men, especially in men with an old age after administration of the Moderna vaccine.

Zhao et al. [9] have reported that urologic complications are rare and that they are more commonly associated with Pfizer/BioNTech vaccine than with Moderna vaccine. Although both vaccines could cause adverse reactions, AEs were reportedly less frequently in the Pfizer/BioNTech vaccine group.

Both Pfizer/BioNTech and Moderna vaccines are licensed vaccines that employ a modified RNA to encode the SARS-CoV-2 spike protein along with mutations in the mRNA added to lock spike proteins into a three-dimensional shape that could naturally bind to human ACE-2 receptor cells with which virus-neutralizing antibodies must interact [27]. Both have a better safety profile than viral vaccines as they are not made of actual pathogens. Thus, they do not integrate into host DNAs.

There is hardly any data pertaining to the mechanism involved in the side effects after a COVID-19 vaccination. The immune response generated by the vaccine could be used to help explain this process. Immune-related pathway is triggered after vaccination which is somehow reflected in a person's urine. A recent study has shown apparent changes in some urinary proteins related to regulated exocytosis and immune response between before and after COVID-19 vaccination [28].

Our study performed an updated analysis of the prevalence of urologic complications following administration of COVID-19 vaccines. There were several limitations in the course of conducting this study. One limitation was that it was difficult to determine what was a true side effect as many symptoms reported were also present in the general population. However, many patients reported symptoms

such as lower urinary tract symptoms could well be part of an immune response generated by the vaccine. Another limitation was that detailed information such as the presence of co-morbidities and so on about subjects of this study was unavailable. Another limitation was the possibility of a reporting bias. For instance, patients who experienced severe reactions after the first dose might have chosen to report their symptoms straight away while those with milder symptoms chose not to report any side effects at all with either dose of the vaccine. In addition, regarding the relationship between COVID 19 vaccine and benign prostatic hyperplasia (BPH) or LUTS, we could not demonstrate a direct connection. Although we could not show relationship between COVID 19 vaccine and BPH/LUTS, recent studies have proposed that LUTS may be increased early symptoms of COVID-19, particularly in older males, may be possible complications of this disease [29]. To date, no study has investigated the potential mechanisms of SARS-CoV-2 in causing BPH related complications, LUTS or exacerbation of a previously diagnosed BPE in severe cases, or asymptomatic carriers of COVID-19, and the underlying mechanisms resulting in this condition as a complication of COVID-19 are not elucidated. One possible mechanism include androgen mediated theory [30], and another theory proposes the possible role of diabetes, cardiovascular dysregulation, and metabolic syndrome in BPH aggravation [31] and SARS-CoV-2 infection. Since the VAERS presents adverse events reported by volunteer reporters, it might not represent the totality of the entire spectrum or quantity of urologic side effects following vaccine administration. One last important limitation we found was that only a limited portion of the US population had been vaccinated up to date.

Conclusion

Based on an updated analysis of available data, it can be concluded that urologic complications following administration of COVID-19 vaccines should not be ignored, although their prevalence is low. However, specific urologic complications such as gross hematuria are not low in incidence. These results strongly suggest that a long-term and detailed follow-up of urologic complications arising after a COVID-19 vaccination is needed to gain a more holistic picture and understand the problem.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00345-023-04481-1>.

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Author contributions SRS: data collection and analysis; KTK: data collection; EP: data management; JHP: manuscript writing; JHK: data management and manuscript editing; BIC: protocol development.

Data availability The data used in this study are publicly available through CDC WONDER (<https://wonder.cdc.gov/controller/datarquest/D8;jsessionid=43405178036DF1F0B4ECA81C1298>).

Declarations

Conflict of interest The author declares that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by the authors.

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