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SHORT COMMUNICATION

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COVID-19 vaccination is associated with a decreased risk of orchitis and/or epididymitis in men

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Abstract

Vaccine hesitancy is a major public health obstacle to fighting the ongoing COVID-19 epidemic. Due to studies that show COVID-19 infection can affect sperm parameters and lead to orchitis, the public are concerned about the effect of the COVID vaccines on male reproduction. In this study, we investigated the association between COVID-19 vaccination and risk of developing orchitis and/or epididymitis outcomes in a cohort of men using a large, US-based, electronic health record database. After balancing for confounding variables, we found that receiving at least 1 COVID-19 vaccine is associated with a decreased risk of developing orchitis and/or epididymitis.

KEYWORDS

COVID-19, COVID-19 vaccine, epididymitis, male fertility, orchitis

1 | INTRODUCTION

Despite the development of three vaccines to combat the ongoing COVID-19 epidemic, vaccine hesitancy remains the primary public health challenge in slowing the spread of the virus in the United States. Currently, the share of Americans fully vaccinated against COVID-19 is just 54%, and 63% have received at least one dose of a two-dose protocol (Ritchie et al., 2020). Americans cite many different reasons for choosing whether or not to become vaccinated, but one of the most common concerns is uncertainty or mistrust of how the COVID-19 vaccine may affect fertility (Diaz et al., 2021; Sajjadi et al., 2021).

The reason for the concern about the negative impact of COVID vaccines on male reproduction is because the COVID-19 virus can adversely affect male fertility (Best et al., 2021) and has been linked to testicular pain/orchitis and epididymitis (Achua et al., 2021; Bridwell et al., 2021; Pan et al., 2020). Alternatively, there is no evidence to show that the COVID-19 vaccines cause problems with male fertility (CDC, 2020). In fact, one study found that there was no significant decrease in sperm parameters after receiving two doses of a COVID-19 mRNA vaccine (Gonzalez et al., 2021). However, no studies have been performed to our knowledge that assesses the effect of COVID-19 vaccination on orchitis and/or epididymitis. In this study, we investigated whether or not receiving a COVID-19 vaccine was independently associated with development of orchitis and/or epididymitis.

2 | METHODS

In this comparative cohort study, we queried data from TriNetX LLC Dataworks Network, a US-based health research network that collects de-identified electronic health record data from 46 health-care organisations and has over 70 million records. The TriNetX platform has been used previously to determine outcomes associated with COVID-19 (Annie et al., 2020; Jorge et al., 2021). We identified male patients ages 12 years and older who received a single-dose COVID-19 vaccine or at least 1 of a 2-dose vaccine regimen using specific ICD-10 medication and procedure codes and compared them with a cohort of men who did not have any COVID-19 vaccine codes in their health record.

The primary outcome for analysis was development of orchitis and/or epididymitis (N45, N45.1, N45.2, N45.3, N45.4 and N51) between 1 and 9 months after the index event of COVID-19 vaccination. Statistical analysis was performed comparing development of orchitis between both cohorts. Odds ratios were calculated both before and after propensity score matching, a technique that utilises logistic regression to construct equivalent cohorts that are matched by potential confounding variables to determine whether any association is independent. We matched the cohorts using the following potentially confounding variables: age, race, urinary tract infection (N39.0) and unspecified sexually transmitted disease (A64) as these variables have been previously identified as risk factors for orchitis independent of receiving the COVID-19 vaccine (Trojian et al., 2009).

All ORs were calculated with associated 95% confidence intervals, and significance was assessed at $p < 0.05$.

3 | RESULTS

We identified 663,774 men in the database who had received at least 1 dose of a COVID-19 vaccine, and 9,985,154 who did not. The mean age in the COVID-19 vaccinated and unvaccinated cohorts was 52.2 and 47.2, respectively. After balancing using propensity score matching, there were 663,774 patients in each cohort.

Prior to propensity score matching, 340 (0.051%) patients in the vaccinated cohort were diagnosed with orchitis and/or epididymitis within the study time period, while 8,257 (0.083%) patients in the unvaccinated cohort had orchitis and/or epididymitis in this time window. In the unbalanced statistical analysis, those who had received a COVID-19 vaccine were significantly less likely to develop the outcome of orchitis and/or epididymitis (OR = 0.619; 95% CI: 0.556–0.690; $p < 0.0001$). After balancing the cohorts for potentially confounding variables, the COVID-19 vaccine remained protective against orchitis and/or epididymitis (OR = 0.568; 95% CI: 0.497–0.649; $p < 0.0001$).

4 | CONCLUSION

In this retrospective cohort study, we demonstrated that receiving a COVID-19 vaccine is associated with a decreased risk of developing orchitis and/or epididymitis. Our findings are consistent with previous studies that have found no relationship between COVID-19 vaccines and adverse male reproductive outcomes (Gonzalez et al., 2021). These findings have important implications in the counselling of patients that are hesitant to receive the COVID-19 vaccine and refute false claims made on social media about the vaccine's effect on male fertility (CDC, 2021). This study was strengthened by a large sample size, control of confounding factors through propensity score matching and control for immortality bias through tight control of outcome time window and diagnosis chronology. As with all retrospective cohort studies using claims databases, this study was limited by potential errors in health record entry, an inability to account for specific symptoms or disease severity and incomplete data or loss to follow-up. Therefore, further studies are needed to validate and expand upon our findings.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from TriNetX, LLC. Restrictions apply to the availability of these data, which were used under licence for this study. Data are available from the authors with the permission of TriNetX, LLC.

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