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Brief Report

COVID-19 vaccination among individuals with autism spectrum disorder: A population-based study

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ABSTRACT

Background: Individuals with autistic spectrum disorder (ASD) are more susceptible to COVID-19 morbidity and should therefore be prioritized for vaccination. Although individuals with neu- rodevelopmental disabilities are given some priority in Israel, it is unclear to what extent individuals with ASD are being vaccinated relative to that of the general population. This study was aimed to assess vaccination prevalence among individuals with ASD.

Method: Individuals with ASD, and age- and sex-matched controls (total $n = 11,080$), were assessed for prevalence of COVID-19 vaccination by February 2021, approximately a month and a half after the national vaccination distribution plan was launched in Israel. Data were obtained from the database of Clalit Health Services (CHS), the largest healthcare organization in Israel.

Results: Individuals with ASD were more likely to be vaccinated for COVID-19 ($OR = 2.55, 95 \% CI 2.35–2.75$, $p < .001$) across both sexes, but only in the 16–20 ($OR = 2.04, 95 \% CI 1.79–2.32$, $p < .001$) and 21–40 ($OR = 3.95, 95 \% CI 3.52–4.43$, $p < .001$) age groups. After adjusting for chronic illnesses, ASD remained significant in predicting the uptake of COVID-19 vaccination.

Conclusions: Efforts to prioritize ASD patients may improve vaccination prevalence among individuals with ASD, especially among younger individuals. Healthcare providers worldwide should therefore consider prioritization policies so as to increase vaccination rates among this vulnerable population.

1. Introduction

With the emergence of the COVID-19 pandemic, concerns have been raised regarding the physical and mental effects of the disease on individuals with autism spectrum disorder (ASD). A recent study conducted by Krieger, Erez, Weinstein, Cohen, and Tzur Bitan, 2021, Krieger, Grossman-Giron et al., 2021) found a higher infection prevalence among individuals with ASD, as well as higher odds for hospitalization. It has been argued that individuals with ASD are prone to physical comorbidities, and are more likely to be infected by COVID-19 due to their difficulty in changing routine and adjusting to public health guidance (Eshraghi et al., 2020). Studies assessing the effect of the pandemic on families with children with ASD reported that parents were challenged by the loss of essential

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services during lockdowns and throughout the pandemic (Neece, McIntyre, & Penning, 2020) and reported parental stress and decreases in emotional well-being during the pandemic (Alhuzimi, 2021). These findings have led to a call for innovative ways to ensure continuity of care for individuals with ASD during the pandemic (Smile, 2020). One such potential way is the prioritization of COVID-19 vaccination for individuals with ASD, so as to enable a fast return to support services which were closed during lockdowns.

Although studies assessing COVID-19 vaccination prevalence across vulnerable groups are scarce, there are some indications of potential disparities even when vaccinations are fully available. Scholars suggest that some people will be less inclined to receive the COVID-19 vaccination because of general vaccine hesitancy, lack of provision of scientific information among the public, as well as other cultural and ethical considerations (Harrison & Wu, 2020). Lower rates of influenza vaccinations, for example, have been previously associated with reduced awareness, fear, or lack of encouragement by primary caregivers (Miles, Williams, Luthy, & Eden, 2020). Nonetheless, to date no study has examined whether individuals with ASD present a similar proportion of vaccination compared to the proportion among the general population.

There is reason to suspect that individuals with ASD might show a differential pattern of vaccination. As individuals with ASD are likely to be supported by their families, as well as by different caregivers in the social support systems (Marsack & Hopp, 2019), it is possible that vaccination will be facilitated by these caregivers, thus resulting in a differential probability for vaccinations compared to the general population. Furthermore, individuals with neurodevelopmental disorders, broadly defined, have been prioritized for COVID-19 vaccination in Israel at ages younger than 16 (Ministry of Health, 2021). At these ages, children were invited by their primary care clinic to be vaccinated. This prioritization may have facilitated parents to vaccinate their children with ASD, regardless of their age.

In this study we aimed to assess the prevalence of COVID-19 vaccination among individuals with ASD in Israel, compared to age- and sex-matched controls. Specifically, we aimed to address the following exploratory questions: (a) Were individuals with ASD vaccinated for COVID-19 to the same extent as their age- and sex-matched counterparts? (b) Were gaps in vaccination specific to sex or age group? (c) Did ASD predict the probability of being vaccinated after adjusting for demographic and clinical risk factors? To answer these research questions, we utilized the database of Clalit Health Services in Israel.

2. Methods

2.1. Data source

The original database was originally mined by the beginning of February 2021 (see Krieger, Erez et al., 2021, Krieger, Grossman-Giron et al., 2021). Vaccination data were obtained from the CHS database by the end of February 2021. In Israel, every citizen of Israel is entitled to healthcare services under the National Health Insurance Law (Ministry of Health, 1994). Healthcare services under this law are provided by four competing not-for-profit health maintenance organizations. Clalit Health Services is the largest healthcare organization of the four, and covers nearly five million citizens, over 50% of the country’s population, through primary healthcare clinics and other medical facilities throughout all regions of the country (Ministry of Health, 2018). Healthcare services are supplied by the governmental sick funds and include a standardized basket of medical services, such as primary care and hospitalization, while supplementary healthcare services with broader coverage are paid by those wishing to expand their insurance. The CHS database is regularly updated with ongoing medical information extracted from primary care clinics, pharmacies, and hospitals. Medical and psychiatric diagnoses are routinely validated by the CHS research groups. In the current study, validation of the ASD diagnoses was performed by author [masked for peer review], who previously reported on a 93% accuracy rate [masked for peer review]. This process included a manual extraction of 150 cases (2.7%) and an examination of the documented clinical presentation, which was followed by a comparison between the clinically validated diagnosis and the diagnosis registered in the CHS database. Overall, a 93% accuracy rate was observed.

Since the outbreak of the COVID-19 pandemic, Israel has experienced four waves, the first one starting in March 2020, and the most recent one starting in June 2021. During the first three waves, the Israeli government ordered lockdowns, including a closure of the education system, social distancing, gathering limitations, and mandatory face masks. Between January 1 st 2020 and August 2nd 2021, there were 880,916 confirmed cases of COVID-19 and 6487 deaths. The mass vaccination plan in Israel was launched at the end of December 2020. Medical staff and individuals above age 60 were given first priority, along with individuals with medical illnesses and residents of nursing homes and social service facilities. During the course of January 2021, the age of prioritization gradually decreased, until full access was granted to all citizens above the age of 16. Individuals aged 16 and above were authorized for vaccination by mid-January 2021, while individuals with neurodevelopmental disabilities under this age were given special authorization and actively invited to be vaccinated by the beginning of February 2021 (Ministry of Health, 2021). Vaccinations were administered at primary healthcare centers as well as at purpose-built vaccination centers. For the purposes of the current study, vaccination was defined as having received at least one vaccine shot. The study was approved by the institutional review board of the institution conducting the study [masked for peer review], where informed consent was waived due to the anonymous nature of data extraction.

2.2. Study population and disease definition

The database was mined in February 2021, approximately a month and a half after the national vaccination distribution plan was launched in Israel. Vaccinations were documented from the onset of the vaccination plan in Israel and up to the date of data extraction. The mined database included 16,779 individuals with ASD, and a group of age- and sex-matched controls, sampled at a 1:1 ratio. After
exclusion of individuals with insufficient data (n = 246) and deceased cases (n = 126), along with their matched controls, the sample included 32,814 individuals. As vaccination was only available for individuals aged 16 and above, all cases below the age of 16 were excluded, along with their control counterparts (n = 21,734). Thus, the analyzed sample for this study included 11,080 participants, with 5540 individuals with ASD and 5540 age- and sex-matched controls (see Fig. 1 for a flowchart of included and excluded cases).

The diagnosis of ASD was based on codes 299 and F84 of the ICD-9 and 10 (pervasive developmental disorders) including the following subtypes: infantile autism (current or active state), disintegrative psychosis, other specified early childhood psychosis, unspecified childhood psychosis, pervasive developmental disorder, childhood autism, atypical autism, Rett syndrome, Asperger’s syndrome, other pervasive developmental disorders, and pervasive developmental disorder unspecified (Krieger, Erez et al., 2021; Rai et al., 2017, Krieger, Grossman-Giron et al., 2021). The ASD diagnoses were based on the registration of either a community psychiatrist or as documented on a discharge letter from a hospital. Diagnosis was registered in any year of life, and only one code was included, along with their control counterparts (n = 11,080, participants, with 5540 individuals with ASD and 5540 age- and sex-matched controls (see Fig. 1 for a flowchart of included and excluded cases).

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2.3. Statistical analysis

Demographic and sociodemographic differences were assessed using chi-square and binary logistic regressions for categorical variables and t-tests for continuous variables. Univariate logistic regressions were employed to test the association between ASD and vaccination, while stratifying to different age and sex groups. Multiple regression analysis was performed to assess the predictive value of different factors that can potentially contribute to the prevalence of vaccination. Statistical analysis was conducted using SPSS software, version 25 (SPSS, Chicago, IL, U.S.A.), with a threshold of p < .05 for statistical significance.

3. Results

Demographic and clinical characteristics of the study sample is described in Table 1.

As can be viewed, significant differences were observed in country of birth and socioeconomic status (SES), where Israeli-born and lower-SES individuals were more prevalent in the control group, χ²(2) = 17.46, p < .001 and χ²(2) = 751.54, p < .001, respectively. There were no significant differences in prevalence of hypertension and diabetes. However, individuals with ASD were significantly less likely to have asthma compared to the control group, χ²(2) = 11.52, p = .001.

Table 2 presents the vaccination prevalence across the two groups. Overall, individuals with ASD were significantly more likely to be vaccinated compared to the control group (OR = 2.55, 95 %CI 2.35–2.75, p < .001). This trend was significant in the 16–21 age group, where 35.9 % of the ASD group were vaccinated compared to 21.6 % in the control group (OR = 2.04, 95 %CI 1.79–2.32, p < .001), and particularly in the 21–40 age group, where 61.8 % of the ASD group were vaccinated compared to only 29 % in the control group (OR = 3.95, 95 %CI 3.52–4.43, p < .001). On the other hand, vaccination prevalence across the at-risk age groups of 40–60 and 60+ was overall higher, ranging from 58.4 %–70.7 %, with no significant differences between the ASD group and the controls. A higher prevalence of vaccination was observed among the ASD group among both male and female participants.

Table 3 presents the results of the multivariate logistic regression analysis predicting probability to be vaccinated by age, sex, SES, diabetes, asthma, hypertension, and ASD diagnosis. After controlling for these covariates, ASD diagnoses remained significant in predicting the probability for being vaccinated. High SES was the largest predictor of probability for being vaccinated (OR = 2.97, 95 %CI 2.66–3.32, p < .001), while ASD diagnosis was the second-largest predictor (OR = 2.22, 95 %CI 2.04–2.42, p < .001), followed by age (OR = 1.05, 95 %CI 1.04–1.05, p < .001). Sex and chronic diseases were not significant predictors after controlling for all other

Fig. 1. Participants’ inclusion and exclusion flow diagram.
4. Discussion

The results of this study indicated a higher vaccination proportion among individuals with ASD in comparison to a randomly selected sample of individuals from the CHS database in Israel. Specifically, it was found that prevalence of vaccination among individuals with ASD was significantly higher compared to the control group, across both male and female participants. This trend was significant especially in the 16–40 age groups, whereas prevalence of vaccination among individuals aged 40 and above was roughly
the same, and relatively higher than that of the younger age groups. ASD diagnosis was predictive of vaccination uptake even after controlling for sociodemographic and clinical factors, and was second in predictive effect after SES.

Although individuals with ASD were not specifically prioritized, the mass vaccination plan in Israel included residents of social service facilities at early stages. This prioritization may have included individuals with autism living in long-term care homes. Furthermore, children with neurodevelopmental disorders below the age of 16 could receive special authorization for early vaccination and were actively invited to receive the vaccination. This rollout may have produced a higher awareness in the public toward the importance of vaccinating this at-risk group at older ages too. The higher observed SES among individuals with ASD, which has also been reported in previous studies (Jo et al., 2015; Thomas et al., 2012), may also explain the higher proportion of vaccination, as previous studies also reported that higher SES was associated with higher vaccination prevalence (Tzur Bitan, Kridin, Cohen, & Weinstein, 2021). Nonetheless, as the higher proportion of vaccination among the ASD group was sustained even after controlling for SES, it is also likely that other contributing factors affected this association. These factors remain to be examined in future studies.

Several reports have recently been published to document prioritization efforts for at-risk populations. Rotenberg et al. (2021) reported on prioritization efforts in Ontario, Canada, which aimed to allow better accessibility to vaccination among individuals with disabilities. They reported that vaccination prevalence was slightly higher for adults with intellectual and developmental disabilities, although the differences were not as great as expected given that all adults with intellectual or developmental disabilities (IDD), regardless of age, were prioritized as a high-risk group during Phase 2. The OpenSAFELY Collaborative et al. (2021) described trends and variations in vaccine coverage by geographic area, and key clinical and demographic patient groups in the UK. They reported that patients with medical conditions were either equally likely, or more likely, to receive vaccination, with two exceptions: those with severe mental illnesses and those with intellectual disabilities. Thus, it appears that there are variations in vaccination prevalence across countries, across time-points and across different diagnostic groups.

The results of the study have several clinical and empirical implications. The results suggest that efforts to prioritize vulnerable groups susceptible to COVID-19 infection and morbidity may be effective in specific circumstances. This is especially true for younger citizens, who are generally less inclined to be vaccinated (Sherman et al., 2020). Future studies should assess whether the high responsiveness of the ASD group toward the COVID-19 vaccination was related to the prioritization of social service facilities, or the presence of guardians or therapeutic agents who allowed easier access to the vaccinations. Such efforts may also be relevant to other vulnerable groups, who are known to be under-vaccinated (Tzur Bitan, 2021), as well as to other countries looking for ways to improve access to vaccination. Future studies should assess whether attempts to increase awareness among other vulnerable groups might improve vaccination prevalence as well.

This study had several limitations. The diagnosis of ASD included a large and heterogeneous group of diagnoses. Future studies should examine whether vaccination prevalence differs across the different diagnosis subtypes, for example across individuals with or without intellectual disabilities. As this was a cross-sectional study, no inference of causal interactions between ASD and vaccinations can be made. The study relied primarily on diagnosis provided in primary healthcare settings. Future studies should assess the replicability of the results using other measures such as self-report or lab results. Differences in vaccination prevalence were assessed at early stages of the vaccination rollout. Future studies should examine whether the observed trends were sustained throughout the period of vaccination administration, using a longitudinal design. Although the diagnosis of ASD underwent a process of validation, the provision of diagnosis is contingent on patients’ request for evaluation through their healthcare provider. Therefore, the possibility that high-functioning cases, or individuals with ASD who were of lower SES, were not evaluated and subsequently under-represented in the CHS registry, cannot be ruled out. The process of validation was performed by an expert psychiatrist. Nonetheless, no inter-rater reliability was obtained, and validation relied only on standard DSM or ICD classification. Additional studies are needed to further validate the reported findings, while taking these limitations into account. Further research is needed to assess whether vaccination proportion varies across individuals with ASD with or without intellectual disabilities. As vaccination accessibility and uptake is likely to be affected by the presence of a caregiver and the type of residential living situation (e.g., independent living versus community home setting), future studies should assess differences in vaccination prevalence while exploring the mediating effect of these factors. As different population groups in Israel (e.g., Arabs and Ultraorthodox Jews) present differential attitudes toward vaccination (Green, Abdullah, Vered, & Nitzan, 2021), as well as differential vaccination rates (Tzur Bitan et al., 2021), future studies should assess whether the results of this study are sustained when taking the population group into account.

5. Conclusions

The results of the current study point to a greater likelihood of obtaining the first vaccine among individuals with ASD in comparison to individuals without such a diagnosis. These differences were observed among male and female participants, and were significant across the age groups of 16–20 and 21–40. In older age groups, no differences were found, and vaccination prevalence was relatively high among both individuals with ASD and controls. Future studies should examine whether efforts to prioritize this at-risk group, or alternatively clinical and demographic factors, may have led to this differential pattern of vaccination. As individuals with ASD are at an increased risk for severe COVID-19 illness (Krieger, Erez et al., 2021, Krieger, Grossman-Giron et al., 2021), efforts should be made to continue and assess vaccination prevalence among these individuals, as well as to examine whether these relatively high rates are sustained over time. Taken together, the results indicate that individuals with ASD are more frequently vaccinated compared to the general population in Israel, and that vulnerable populations can receive sufficient medical care even in the age of a pandemic if given the appropriate accessibility. Such findings have important implications for prioritization policies worldwide.
Contributors

Orly Weinstein: Conceptualization, Data curation, Writing- Reviewing and Editing. Israel Krieger: Conceptualization, Methodology, Writing- Reviewing and Editing.

Arnon Dov Cohen: Conceptualization, Methodology, Writing- Reviewing and Editing. Dana Tzur Bitan: Writing- Original draft preparation, Methodology, Investigation, Writing- Reviewing and Editing.

Declaration of Competing Interest

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