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Comparative Analysis of Adverse Drug Reactions (ADRs) between COVID-19 Vaccines and Established Vaccines: A CDC VAERS Database Analysis

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ABSTRACT

Background: COVID-19 vaccines have been developed rapidly to combat the pandemic, but vaccine hesitancy remains a challenge due to concerns about adverse drug reactions (ADRs). This study aimed to compare the ADR profiles of COVID-19 vaccines with established vaccines and investigate differences between adults and children. **Methods:** A retrospective observational study used the VAERS database to analyze ADR reports from January 2021 to December 2022 in the United States. Top ten common ADRs and seven severe ADRs associated with COVID-19 vaccines were studied using the Evans Criteria. **Results:** Among the common ADRs, only dyspnea showed disproportionate reporting in COVID-19 vaccines. Severe ADRs, including myocarditis, pneumonia, and cerebrovascular accidents, were disproportionately reported. Age-stratified analysis revealed myocarditis disproportionately reported in both adults and children. **Conclusions:** This study provides a comprehensive comparison of ADRs between COVID-19 vaccines and established vaccines. Although some severe ADRs were disproportionately reported, further evaluation is required to establish any causal relationships with COVID-19 vaccine. Continuous monitoring of ADRs is crucial for vaccine safety.

Introduction

The COVID-19 pandemic, which emerged during 2019-20, rapidly spread worldwide, prompting the World Health Organization (WHO) to declare it a global pandemic. Vaccines stand as one of the most significant accomplishments in public health and their implementation has led to a substantial reduction in mortality and the severity of symptoms associated with numerous infectious diseases (Vetter et al., 2017). In response to the pandemic, extensive efforts were initiated to develop effective vaccines, aiming to curtail infection rates and halt further transmission (Vetter et al., 2017, Orenstein & Ahmed, 2017,). Globally, more than 125 vaccine candidates were created and around 365 vaccine clinical trials were conducted (Sallam, 2021). In the United States (US), the Food and Drug Administration (FDA) approved four vaccines for use: Moderna, Pfizer-BioNTech, Novavax, and Janssen/Johnson & Johnson vaccine (Mayo Clinic, 2021). The effectiveness of these vaccines was tested thoroughly through multiple clinical trials before being approved by the FDA. In late 2020, the first COVID-19 vaccine was authorized for public use in the US (CDC, 2022).

Despite the development of COVID-19 vaccines, the public's willingness to receive them has been met with hesitancy (Dubé et al., 2013.). For instance, in the United States (US), earlier surveys indicated that only 50 percent of respondents were inclined to receive the COVID-19 vaccines (Guidry et al., 2021). Vaccine hesitancy toward the COVID-19 vaccines is influenced by several factors, including concerns about their safety (Troiano & Nardi, 2021). In Canada, a significant cause of hesitancy stems from the belief that the vaccines contain potentially harmful ingredients or may lead to other health complications (Griffith et al., 2021). Likewise, in the US, apprehension about vaccine safety and potential adverse reactions (ADRs) has been a major factor contributing to hesitancy among the public (Sallam, 2021). Other factors include lack of familiarity with vaccine-preventable diseases, compulsory nature of

vaccines, socio-demographic characteristics, cultural beliefs, and distrust in corporations and public health agencies (Salmon et al., 2015, Dror et al., 2020). Traditionally, the process of vaccine development involves several phases of rigorous clinical trials and extensive safety and efficacy evaluations, which can take 10-15 years before receiving authorization for public use. However, the development timeline for COVID-19 vaccines was notably accelerated, and novel technologies were utilized to meet the urgent global need for effective immunization against the virus (Singh, Khillan, & Mishra, 2022). Many vaccine-hesitant individuals are worried that normal regulations were not followed in the creation of the COVID-19 vaccines due to the urgent need to make them available to the public. The WHO Strategic Advisory Group of Experts (SAGE) on Immunization concluded that vaccine hesitancy is defined as the refusal or delay of vaccination despite access to safe vaccines (MacDonald, 2015). WHO SAGE group describes hesitancy as related to three main factors, the '3C's of vaccine hesitancy': confidence, complacency, and convenience" (WHO, 2021, p. 4). Confidence refers to the individual's trust in the safety and effectiveness of the vaccine and in the healthcare system and policy-makers that promote them (WHO, 2021). Complacency refers to an individual's belief that vaccination is not needed due to the minimal risk of being infected (WHO, 2021). Finally, convenience refers to whether or not an individual has access to vaccines (WHO, 2021).

Vaccine hesitancy poses a significant threat to public health, especially for vulnerable populations such as the elderly and immunocompromised. Achieving herd immunity, a critical milestone in disease control, becomes increasingly challenging when a sizable portion of the community remains hesitant or resistant to vaccination (WHO, 2020). Vaccine hesitancy also leads to more severe symptoms of COVID-19 infection in unvaccinated individuals as the vaccine has the ability to lessen the severity of the symptoms experienced after contracting the disease. Studies have indicated that countries with higher levels of vaccine hesitancy experienced significantly higher mortality rates due to COVID-19 (Mesa et al., 2021)

Existing studies on the safety of COVID-19 vaccines have primarily focused on adverse drug reactions (ADRs) following vaccination (Kouhpayeh & Ansari, 2022). The Centers for Disease Control (CDC) (2021) defines an adverse reaction as any untoward or unfavorable medical occurrence following vaccination. The CDC recognizes the importance of monitoring and analyzing ADRs as a primary method to determine vaccine safety (CDC, 2018). However, there is a notable gap in the literature concerning a comprehensive comparison of the safety profiles of COVID-19 vaccines against well-established vaccines that have been used over an extended period. In contrast to well-established vaccines like the Measles, Mumps, and Rubella (MMR) vaccine, COVID-19 vaccines lack long-term efficacy data and have not undergone extensive testing due to the urgent need for a pandemic response. While some research has compared the incidence of anaphylaxis between COVID-19 vaccines and other vaccines (Rodriguez-Nava et al., 2021), few studies have taken a holistic approach to explore the full spectrum of ADRs associated with COVID-19 vaccination and their potential differences compared to other vaccines. There remains a need for comprehensive studies that compare the holistic ADR profiles of these vaccines to those of long-standing, established vaccines. Therefore, the objective of this study was to investigate the ADRs of the COVID-19 vaccines compared to other commonly used vaccine. Our study hypothesis was the rate of ADRs of the COVID-19 vaccines will be similar to other commonly used vaccines.

Methods

Study Design

In this retrospective observational study, we investigated the differences in adverse drug reactions (ADRs) between COVID-19 vaccines and other vaccines using the CDC Wide-ranging Online Data for Epidemiologic Research (CDC WONDER) platform. CDC WONDER is an accessible health information system widely available to professionals and the public without any regulatory permissions (CDC, 2022). We specifically utilized the Vaccine Adverse Event Reporting System (VAERS) database from the CDC WONDER interface (CDC, 2023), which continually monitors vaccine safety after FDA authorization for use in the United States (CDC, 2022). The VAERS database comprises

publicly available and anonymous ADR information reported by clinicians, patients, and vaccine manufacturers (Singh et al., 2023). The study ensured strict adherence to data anonymity and personal information protection. The selection of the VAERS database was based on its versatility, simplicity, and the ability to access up-to-date ADR reports (Rodriguez-Nava et al., 2021), providing a valuable resource for investigating ADRs associated with different vaccine types, including COVID-19 vaccines.

Study Population

Participants who received any vaccine within the timeframe of January 1, 2021, to December 31, 2022, were eligible for inclusion in the study. This period was selected as the COVID-19 vaccines received approval for public use in December 2020, and they became available to the general population from the following year onwards (Mayo Clinic, 2022). To ensure data consistency, only individuals from the US were considered, as the VAERS database exclusively captures cases reported within the US. Regardless of age or gender, all reports of adverse drug reactions (ADRs) were comprehensively assessed from the study population. This approach aimed to provide a comprehensive and inclusive understanding of the overall ADR rate associated with different vaccines during the specified period.

Study Procedure

In order to assess potential statistically significant differences in ADRs between COVID-19 vaccines and other vaccines, a focused analysis of the top ten most common ADRs and seven severe ADRs was conducted. The top ten most common ADRs were selected as they provide valuable insights into the safety profile of a vaccine, representing the most likely adverse events following vaccination (Nelly, 2021). The top ten common ADRs under study were identified as follows: headache, fatigue, pyrexia (fever), pain, chills, dizziness, nausea, dyspnea (shortness of breath), arthralgia (joint pain), and myalgia (muscle pain). Additionally, the study looked at the top seven severe ADRs that have been previously reported to be linked with COVID-19 vaccines to determine if the rate of these severe ADRs is disproportionately higher in COVID-19 vaccines compared to other vaccines. The selected severe ADRs included: anaphylaxis, myocarditis, pericarditis, Guillain-Barre syndrome, pneumonia, uveitis, vasculitis, and cerebrovascular accidents (Simnani, Singh, & Kaur, 2021).

First, the COVID-19 vaccines were selected from the list of vaccines on the VAERS database by all manufacturers (**Appendix A**). Next, the number of total cases of each desired ADR was manually extracted from the unstructured adverse event descriptions and inputted into a google spreadsheet for data analysis. The same approach was employed to gather data for all other vaccines present in the VAERS database. The above data was also analyzed separately for adults and children to see if there were any differences between the two groups in terms of ADRs. Children were classified as individuals aged 5-18 (since children under five were not authorized to receive the COVID-19 vaccines until June 2022) and adults were classified as individuals aged above 18.

Data Analysis

To evaluate the disproportionate reporting of ADRs of the COVID-19 vaccines compared to that of other vaccines, the Evans Criteria was used, which consists of three criteria: a proportional reporting ratio (PRR) greater than or equal to 2 (where PRR is a/[a+c] divided by b/[b+d] in a 2-by-2 proportionality table) , chi-squared ≥ 4 with Yates correction (adjustment for low frequencies), and ≥ 3 cases (Evans et al., 2001). The Evans Criteria was chosen for this study because it is 'one way to determine whether the number of cases reported spontaneously exceeds what might be expected through a combination of chance and background noise' (Evans et al., 2001, p. 5). Although the study done by Evans et al. (2001) sought to detect differences in ADRs for certain drug medications, the same approach has previously used to analyze differences in ADRs of vaccines (Rodriguez-Nava et al., 2021). A disproportionate signal indicating that there is a significant difference for a specific ADR from COVID-19 vaccines is determined if all three

criteria are met (Evans 2001, Shimabukuro, 2015). The PRR values are measures of the strength of association and the greater the PRR value, the higher the strength of the association between a specific ADR and the COVID-19 vaccines. The Evans Criteria was calculated individually for each ADR for the whole study population and further in both adult and children separately to determine if there were any significant differences between the two age groups. The PRR value was calculated by using a 2x2 table. Statistical association was measured using a chi-squared test. The data was inputted into an online statistical calculator which calculated the rate and the chi-squared value with Yates correction (VassarStats, 2001).

Results

A total of 780,547 ADR reports were found for COVID-19 vaccines (all manufacturers), and 37,477 ADR reports were identified for all other vaccines during the two-year study period (January 2021- December 2022) (**Appendix B and C**).

Table 1: Rate of each of the top ten most common ADRs reported after COVID-19 vaccines and all other vaccines

ADR	COVID-19 Vaccines	All Other Vaccines
Headache	15.72%	11.03%
Fatigue	13.78%	9.54%
Pyrexia	13.64%	11.06%
Pain	11.75%	12.09%
Chills	11.27%	8.89%
Dizziness	9.06%	6.75%
Nausea	8.91%	7.24%
Dyspnea	5.93%	2.68%
Myalgia	5.52%	4.29%
Arthralgia	5.50%	5.17%

Abbreviations: ADR: Adverse drug reactions

Table 1 shows the rate of each of the top ten most common ADRs reported after COVID-19 vaccines and all other vaccines. The rate of common ADR in COVID-19 vaccines ranged from 5.50% to 15.72% while it ranged 5.17% to 11.03% in all other vaccines. Headache had the highest rate in both COVID-19 vaccines and all other vaccines.

Table 2: Evan's criteria analysis for ten most common ADRs reported after COVID-19 vaccines

ADR	PRR	$\chi 2$ With Yates Correction	No. of Individual Cases	Meets Evans Criteria?
Headache	1.43	600.17	122,737	No
Fatigue	1.44	548.19	107,585	No
Pyrexia	1.23	204.44	106,504	No
Pain	0.97	3.96	91,731	No
Chills	1.27	61.41	87,997	No
Dizziness	1.34	233.49	70,712	No
Nausea	1.23	123.25	69,540	No
Dyspnea	2.21	691.35	46,267	Yes
Myalgia	1.29	105.04	43,119	No

Arthralgia	1.07	7.76	42,952	No

Abbreviations: ADR: Adverse drug reactions, PRR: Proportional reporting ratio. Evans Criteria for signal detection: PRR ≥2, the $\chi 2$ ≥4, and number of individual cases ≥3.

Table 2 displays the Evan's criteria analysis for the ten most common ADRs of the COVID-19 vaccines. The PRRs ranged from 0.97 to 2.21. Pain had the lowest PRR of 0.97 while Dyspnea had the highest PRR of 2.21. Nine out of the ten ADRs studied were found to have no disproportionate reporting in COVID-19 vaccines compared to all other vaccines per Evan's criteria. Dyspnea was the only common ADR found to have a disproportionate reporting in COVID-19 vaccines.

Table 3: Rate of severe ADRs reported after COVID-19 vaccines and all other vaccines

ADR	**COVID-19 Vaccines**	**All Other Vaccines**
Anaphylaxis	0.22%	0.18%
Myocarditis	0.32%	0.07%
Guillain-Barré Syndrome	0.10%	0.28%
Pneumonia	0.52%	0.19%
Uveitis	0.02%	0.02%
Vasculitis	0.03%	0.03%
Cerebrovascular Accident	0.44%	0.13%

Abbreviations: ADR: Adverse drug reactions

Table 3 shows the rate of each of the seven severe ADRs that have been commonly associated with the COVID-19 vaccines. The reported rates of severe ADRs were much less than the common ADRs in both COVID-19 and all other vaccine groups. The rate of severe ADRs ranged from 0.02 to 0.44% with COVID-19 vaccines while it ranged 0.02 to 0.28% in all other vaccines. Cerebrovascular accidents had the highest rate in COVID-19 vaccines (0.44%) while Guillain-Barre Syndrome had the highest rate in all other vaccines (0.28%).

Table 4: Evan's criteria analysis for severe ADRs reported after COVID-19 vaccines

ADR	**PRR**	**$\chi 2$ With Yates Correction**	**No. of Individual Cases**	**Meets Evans Criteria?**
Anaphylaxis	1.23	2.5	1,710	No
Myocarditis	4.27	68.8	2,491	Yes
Guillain-Barré Syndrome	0.36	104.83	795	No
Pneumonia	2.71	76.16	4,066	Yes
Uveitis	0.87	0.04	164	No
Vasculitis	0.99	0.02	227	No
Cerebrovascular Accident	3.43	80.93	3,425	Yes

Abbreviations: ADR: Adverse drug reactions, PRR: Proportional reporting ratio. Evans Criteria for signal detection: PRR ≥2, the $\chi 2$ ≥4, and number of individual cases ≥3.

Table 4 displays the Evan's criteria analysis for the seven severe ADRs previously associated with the COVID-19 vaccines. The PRRs ranged from 0.36 to 4.27. Guillain-Barre Syndrome had the lowest PRR of 0.36 while

Myocarditis had the highest PRR of 4.27. Myocarditis, pneumonia, and cerebrovascular accidents were found to have disproportionate reporting with COVID-19 vaccines. There was no disproportionate reporting of anaphylaxis, Guillain-Barre syndrome, uveitis, and vasculitis in COVID-19 vaccines compared to all other vaccines.

Table 5: Rate of each of the top ten most common ADRs reported after COVID-19 vaccines and all other vaccines stratified by age.

ADR	COVID-19 Vaccines		All Other Vaccines	
	Adults*	Children**	Adults*	Children**
Headache	16.38%	5.74%	12.24%	5.37%
Fatigue	14.41%	4.27%	10.86%	3.35%
Pyrexia	14.16%	5.85%	12.46%	4.46%
Pain	12.34%	2.84%	13.92%	3.49%
Chills	11.87%	2.20%	10.45%	1.54%
Dizziness	9.15%	7.68%	6.46%	8.10%
Nausea	9.19%	4.70%	7.65%	5.33%
Dyspnea	6.14%	2.64%	2.97%	1.34%
Myalgia	5.83%	0.88%	5.05%	0.73%
Arthralgia	5.82%	0.70%	6.00%	1.25%

Abbreviations: ADR: Adverse drug reactions. *Adults = Ages 18+ **Children = Ages 5-18

The data collected on the top ten ADRs were then stratified by age to determine if there were any differences in occurrence of ADRs between adults and children. The rate of common ADR symptoms reported in adults and children is shown in **Table 5**. The rate of occurrence of common symptoms was higher in adults compared to children in all categories.

Table 6: Evan's criteria analysis for ten most common ADRs reported after COVID-19 vaccines stratified by age

ADR	PRR		χ2 With Yates Correction		No. of Individual Cases		Meets Evans Criteria?	
	Adults	Children	Adults	Children	Adults	Children	Adults	Children
Headache	1.34	1.07	374.95	1.37	119,966	2,771	No	No
Fatigue	1.33	1.28	306.17	12.15	105,522	2,063	No	No
Pyrexia	1.14	1.31	70.55	20.67	103,678	2,826	No	No
Pain	0.89	0.82	68.22	8.24	90,359	1,372	No	No
Chills	1.14	1.43	57.63	11.9	86,935	1,062	No	No
Dizziness	1.42	0.95	259.73	1.33	67,002	3,710	No	No
Nausea	1.20	0.88	84.38	4.81	67,269	2,271	No	No
Dyspnea	2.07	1.97	528.99	39.77	44,993	1,274	Yes	No
Myalgia	1.16	1.21	33.13	1.38	42,693	426	No	No
Arthralgia	0.97	0.56	1.7	22.6	42,616	336	No	No
Headache	1.34	1.07	374.95	1.37	119,966	2,771	No	No

Abbreviations: ADR: Adverse drug reactions, PRR: Proportional reporting ratio. *Adults = Ages 18+ **Children = Ages 5-18, Evans Criteria for signal detection: PRR ≥2, the $\chi 2$ ≥4, and number of individual cases ≥3.

Table 6 shows the Evan's criteria analysis for the ten most common ADRs of the COVID-19 vaccines stratified for age. In adults, dyspnea was the only one to have a disproportionate reporting in COVID-19 vaccines, while, in children, none of the ten common ADRs met the Evans Criteria for disproportionate reporting.

Table 7: Rate of severe ADRs reported after COVID-19 vaccines and all other vaccines stratified by age.

ADR	COVID-19 Vaccines		All Other Vaccines	
	Adults*	Children**	Adults*	Children**
Anaphylaxis	0.22%	0.14%	0.16%	0.26%
Myocarditis	0.26%	1.18%	0.07%	0.11%
Guillain-Barré Syndrome	0.11%	0.05%	0.31%	0.14%
Pneumonia	0.55%	0.06%	0.23%	0.03%
Uveitis	0.02%	0.02%	0.03%	0.02%
Vasculitis	0.03%	0.02%	0.03%	0.03%
Cerebrovascular Accident	0.47%	0.03%	0.15%	0.02%

Abbreviations: ADR: Adverse drug reactions. *Adults = Ages 18+ **Children = Ages 5-18

Table 7 shows the rate of seven severe ADRs stratified by age. The rate of severe ADRs in adults were greater than or equal to the rate in children for all ADRs except for myocarditis which was higher in children.

Table 8: Evan's criteria analysis for severe ADRs reported after COVID-19 vaccines stratified by age

ADR	PRR		χ2 With Yates Correction		No. of Individual Cases		Meets Evans Criteria?	
	Adults	Children	Adults	Children	Adults	Children	Adults	Children
Anaphylaxis	1.42	0.54	5.52	4.69	1,643	67	No	No
Myocarditis	3.86	11.06	46.17	62.92	1,922	569	Yes	Yes
Guillain-Barré Syndrome	0.34	0.38	111.99	*	770	25	No	*
Pneumonia	2.43	2.11	57.78	*	4,035	31	Yes	*
Uveitis	0.82	1.22	0.13	*	155	9	No	*
Vasculitis	1.01	0.75	0.02	*	216	11	No	*
Cerebrovascular Accident	3.06	2.18	63.95	*	3,409	16	Yes	*

Abbreviations: ADR: Adverse drug reactions, PRR: Proportional reporting ratio. *Adults = Ages 18+ **Children = Ages 5-18, Evans Criteria for signal detection: PRR ≥2, the $\chi 2$ ≥4, and number of individual cases ≥3.

Table 8 shows the Evan's criteria analysis for the seven severe ADRs stratified by age. The Evans Criteria was not able to be applied for five of the severe ADRs in children due to an extremely small number of cases reported (**Appendix C**). The small number of cases resulted in the statistical calculator not being able to accurately calculate the chi-squared value, which is necessary to determine if the Evans Criteria is met. No disproportionate reporting was found for anaphylaxis while myocarditis was disproportionately reported in COVID-19 vaccines for both adults and children.

Discussion

The goal of this study was to compare the ADRs of the COVID-19 vaccines versus those of other vaccines in order to determine if any ADRs were disproportionately reported for the COVID-19 vaccines. The VAERS database was utilized to gather data on ADRs and the data collected was analyzed using the Evans Criteria. This study was the first to research the holistic ADR profile of the COVID-19 vaccines compared to that of other vaccines as well as analyze the data separately in adults and children. It was found that most ADRs were not disproportionately reported, but few were, indicating need for further evaluation.

Of the ten most common ADRs, dyspnea was the only ADR with a statistically significant higher reporting with COVID-19 vaccines (PRR 2.21, **Table 2**), compared to all other vaccines. The rest of the common ADRs, including headache, fatigue, pyrexia, pain, chills, dizziness, nausea, arthralgia, and myalgia were not disproportionately reported (PRR < 2) for COVID-19 vaccines compared to all other vaccines (**Table 2**). These findings are consistent with previous studies that observed that ADRs, such as pain, tiredness, headaches, muscle/joint ache, and chills are common to all vaccines, and typically occur as a result of a normal immune system response (El-Shitany et al., 2022). Many of the top ten common ADRs of the COVID-19 vaccines were consistent with the normal immune reaction of the body following any type of vaccination, plausibly the reason for no disproportionate reporting. It was found, however, that the rate of occurrence for the top ten common ADRs was slightly higher in COVID-19 vaccines compared to all other vaccines (**Table 1**). One reason for the higher rates of common ADRs with COVID-19 vaccination as compared with other vaccines potentially secondary to reporting bias that is triggered by public anxiety due to the novelty of COVID-19 vaccines (Riad et al., 2022, p. 30). The age-stratified analysis showed that dyspnea was disproportionately reported only in adults and not in children. It is likely that the underlying comorbidities in adults may predisposing to higher incidence of dyspnea (Simnani, Singh, & Kaur, 2021). The disproportionate reporting of dyspnea in COVID-19 vaccines indicates that this particular ADR may be a signal for further evaluation, especially in adults.

Of the severe ADRs, myocarditis, pneumonia, and cerebrovascular accidents were reported higher with COVID-19 vaccines (PRRs of 4.27, 2.71, and 3.43 respectively, **Table 4**). The rest of the severe ADRs associated previously with the COVID-19 vaccines including anaphylaxis, pericarditis, Guillain-Barre syndrome, uveitis, and vasculitis were not found to be disproportionately reported in COVID-19 vaccines. The disproportionate reporting of myocarditis is also reported by another study which observed that there is a slight increase in risk of myocarditis after receiving COVID-19 vaccines (Oster, Shay, & Shimabukuro, 2022). The disproportionate reporting of cerebrovascular accidents indicates a signal for further evaluation. A prior study investigating the neurological ADRs of the COVID-19 vaccines concluded that these are often isolated events that may occur because of differences in genetic makeup that lead to autoimmune reactions (Patone et al., 2021). They also reported that the risk of neurological complications with COVID-19 infection exceeds that of all the COVID-19 vaccines (Patone et al., 2021, p. 2153). There are currently no studies that reported an association between the occurrence of pneumonia following COVID-19 vaccination, which also indicate the need for further evaluation of this ADR. Our age-stratified analysis showed that myocarditis is disproportionately reported both in adults and children, but children have higher PRR compared to adults (11.06 vs. 3.89, **Table 8**). It was noted in another study that myocarditis cases following vaccination were most common in adolescents aged 12-17 years old, with no clear explanations (Klein et al., 2021).

Numerous concerns were raised about Covid-19 vaccines due to the emergency situation in which they were developed, resulting in vaccine hesitancy (Anand & Stahel, 2021). The results of this study show that most ADRs studied did not have disproportionate reporting in COVID-19 vaccines and that for the ADRs that did have disproportionate reporting, the rate of occurrence was less than 0.6% for severe ADRs and 6% for common ADRs. This information can assist in informed risk-benefit decision-making regarding vaccination. The study also found that myocarditis, pneumonia, and cerebrovascular accidents had disproportionately higher reporting in association with COVID-19 vaccines. This signals the need for further evaluation to determine any potential causal relations between these specific ADRs and the vaccines. On the positive side, the study identifies ADRs that did not show disproportionate

reporting with COVID-19 vaccines. This information can be valuable for healthcare professionals and researchers in avoiding unnecessary investigations into ADRs with weak associations to the vaccine. While the study observes a slightly higher risk of severe ADRs with COVID-19 vaccines, it emphasizes that this cannot be used as an argument against vaccination. The benefits of vaccination in preventing severe outcomes and mortality from COVID-19 far outweigh the minimal and rare risks of vaccination-related ADRs (Piché-Renaud, Morris, & Top, 2022). It is important to note that associations flagged by the Evans criteria do not imply causal relationships, but rather indicate ADRs that require further scrutiny for a better understanding of their relationship to the vaccines (Evans et al., 2001).

Limitations

One significant limitation of this study is that the data was obtained from a passive reporting system, which is susceptible to various inconsistencies such as underreporting or incomplete reporting (Shimabukuro, 2015). Although the CDC mandates that all vaccine-associated adverse drug reactions (ADRs) should be reported by healthcare professionals and vaccine manufacturers, many cases of ADRs are often not reported or delayed, which may have resulted in some reports being overlooked (CDC, 2022). Moreover, the VAERS database may contain inaccurate, incomplete, or coincidental reports of ADRs following vaccination. ADRs are required to be reported to VAERS regardless of concrete evidence linking them to the vaccine, which may lead to the inclusion of uncertain cases. Additionally, the information in the VAERS database is not professionally verified, and the data query terms in the request form may be overly nonspecific and broad, potentially causing an overestimation of the database numbers. Despite these limitations, the VAERS database remains a valuable tool for generating signals about vaccine safety and providing ADR data for informed decision-making regarding new vaccines (Rodriguez-Nava et al., 2021).

Areas of Further Research

Further research should focus on individually comparing each FDA-approved COVID-19 vaccine to other vaccines to gain a deeper understanding of their unique properties and adverse drug reactions (ADRs). A study found a masking effect when comparing COVID-19 vaccines, indicating that certain vaccines may be more associated with specific ADRs. Investigating the safety profile of each vaccine can help healthcare professionals and the public make informed decisions when choosing COVID-19 vaccines. Additionally, exploring how different demographic factors, such as ethnicity and gender, affect the occurrence of ADRs after vaccination could shed light on the reasons behind vaccine hesitancy among specific populations. Understanding these factors will be crucial in addressing concerns and promoting vaccine acceptance.

In conclusion, this study aimed to compare the ADRs of COVID-19 vaccines to other commonly used vaccines and evaluate potential differences between adults and children. The findings revealed that most ADRs were not disproportionately reported in COVID-19 vaccines compared to other vaccines. However, some severe ADRs, such as myocarditis, pneumonia, and cerebrovascular accidents, were found to be disproportionately higher in association with COVID-19 vaccines. These signals warrant further investigation to determine if there is a causal relationship between these specific ADRs and COVID-19 vaccines. The study highlights the importance of monitoring and analyzing ADRs to ensure vaccine safety and make informed risk-benefit decisions. It is essential to consider these findings in the context of the greater benefit of vaccination in preventing severe COVID-19 outcomes and reducing mortality rates.

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