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MULTIPLE SCLEROSIS: APPEARANCE AFTER COVID VACCINATION

ESCLEROSIS MULTIPLE: APARICIÓN POSTERIOR A VACUNACIÓN

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Multiple Sclerosis: Appearance after Covid Vaccination

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ABSTRACT

Background: Multiple sclerosis (MS) is a chronic autoimmune disease that primarily affects the central nervous system, often emerging in young adults. In the context of the global COVID-19 vaccination campaign, concerns have been raised about the potential link between vaccination and autoimmune conditions, including MS. This study aims to assess the incidence of MS post-COVID-19 vaccination across different age groups and vaccine types, with a specific focus on identifying at-risk populations. **Methods:** A retrospective cohort study was conducted using publicly available registries, case reports, and clinical data. The study included 450 individuals who developed MS after receiving a COVID-19 vaccine, with an analysis performed on incidence rates, relative risk (RR), and demographic factors such as age, sex, and vaccine type. The data was compared with a control group of 3,000 vaccinated individuals without MS onset. **Results:** The overall incidence of MS among vaccinated individuals was 15 per 100,000. Adults aged 18-40 years had the highest incidence (18 per 100,000), while children under 12 had the lowest (3 per 100,000). Females were disproportionately affected, accounting for 63.3% of MS cases, with an incidence of 18 per 100,000 compared to 12 per 100,000 in males. A higher proportion of cases were linked to mRNA vaccines, particularly Pfizer-BioNTech (54.4% of total cases), though no statistically significant difference was observed among vaccine types. The relative risk of MS in vaccinated adults was 1.35 (95% CI: 1.12-1.60) compared to the general population. **Conclusion:** While there is a slight increase in the incidence of MS among adults following COVID-19 vaccination, particularly with mRNA vaccines, the overall risk remains low. No significant increase in MS risk was observed in younger populations. The benefits of vaccination against severe COVID-19 far outweigh the potential risks of MS onset. Ongoing surveillance and further research are essential to better understand vaccine-related autoimmune responses.

***Keywords*:** multiple sclerosis, COVID-19 vaccination, autoimmune disease, mRNA vaccines, vaccine safety, epidemiology, immune response, autoimmune triggers

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Esclerosis Multiple: Aparición posterior a Vacunación

RESUMEN

Antecedentes: La esclerosis múltiple (EM) es una enfermedad autoinmune crónica que afecta principalmente al sistema nervioso central y suele aparecer en adultos jóvenes. En el contexto de la campaña global de vacunación contra COVID-19, han surgido preocupaciones sobre el posible vínculo entre la vacunación y condiciones autoinmunes, incluida la EM. Este estudio tiene como objetivo evaluar la incidencia de EM posterior a la vacunación contra COVID-19 en diferentes grupos de edad y tipos de vacunas, con un enfoque específico en la identificación de poblaciones en riesgo. **Métodos:** Se realizó un estudio de cohorte retrospectivo utilizando registros públicos, informes de casos y datos clínicos. El estudio incluyó a 450 individuos que desarrollaron EM tras recibir una vacuna contra COVID-19, y se realizó un análisis de las tasas de incidencia, el riesgo relativo (RR) y factores demográficos como la edad, el sexo y el tipo de vacuna. Los datos se compararon con un grupo de control de 3,000 individuos vacunados sin aparición de EM. **Resultados:** La incidencia general de EM entre los vacunados fue de 15 por cada 100,000. Los adultos de entre 18 y 40 años presentaron la mayor incidencia (18 por cada 100,000), mientras que los niños menores de 12 años mostraron la menor incidencia (3 por cada 100,000). Las mujeres fueron afectadas de manera desproporcionada, representando el 63.3% de los casos de EM, con una incidencia de 18 por cada 100,000 en comparación con 12 por cada 100,000 en hombres. Una mayor proporción de casos se vinculó con las vacunas de ARNm, particularmente Pfizer-BioNTech (54.4% del total de casos), aunque no se observó una diferencia estadísticamente significativa entre los tipos de vacunas. El riesgo relativo de EM en adultos vacunados fue de 1.35 (IC 95%: 1.12-1.60) en comparación con la población general. **Conclusión:** Aunque se observa un ligero aumento en la incidencia de EM entre los adultos después de la vacunación contra COVID-19, especialmente con las vacunas de ARNm, el riesgo general sigue siendo bajo. No se observó un aumento significativo del riesgo de EM en las poblaciones más jóvenes. Los beneficios de la vacunación contra la COVID-19 grave superan con creces los posibles riesgos de aparición de EM. La vigilancia continua y una mayor investigación son esenciales para comprender mejor las respuestas autoinmunes relacionadas con la vacunación.

Palabras clave: esclerosis múltiple, vacunación contra COVID-19, enfermedad autoinmune, vacunas de ARNm, seguridad de las vacunas, epidemiología, respuesta inmunitaria, desencadenantes autoinmunes

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INTRODUCTION

Multiple Sclerosis (MS) is a chronic autoimmune disease characterized by the demyelination of neurons in the central nervous system, leading to a wide range of neurological symptoms. The etiology of MS is complex, involving both genetic predispositions and environmental factors, such as viral infections, vitamin D deficiency, and smoking (Goldenberg, 2012). The onset of MS typically occurs between the ages of 20 and 40, and it is more prevalent in women than men (Lublin et al., 2014).

Since the rollout of COVID-19 vaccines, there have been reports of autoimmune conditions, including MS, occurring after vaccination (Mehrotra et al., 2021). Although these cases are rare, they have raised concerns among healthcare professionals and the public alike. Understanding the potential relationship between COVID-19 vaccines and the onset of MS in different age groups, including adults, children, and adolescents, is critical for guiding public health policies and patient care.

This study seeks to explore the appearance of MS in these populations following COVID-19 vaccination. By reviewing current literature, analyzing case studies, and assessing clinical reports, we aim to determine if there is a significant link between vaccination and the onset of MS or if these cases are coincidental.

Literature Review

Multiple Sclerosis Overview

Multiple Sclerosis (MS) is one of the most prevalent autoimmune diseases affecting the central nervous system. It is estimated that approximately 2.8 million people worldwide suffer from MS, with variations in prevalence according to geographical location, ethnicity, and environmental factors (Compston & Coles, 2008). The disease manifests through a variety of symptoms, such as motor dysfunction, cognitive impairments, and sensory disturbances, which can lead to significant disability (Reich et al., 2018).

The pathophysiology of MS is characterized by the immune system mistakenly attacking the myelin sheath, the protective layer around nerve fibers. While the exact triggers for this autoimmune response remain unclear, there is evidence suggesting that both environmental factors and genetic susceptibility contribute to the development of the disease (Dendrou, Fugger, & Friese, 2015). Recent studies also point to viral infections, particularly Epstein-Barr virus (EBV), as a possible environmental trigger for

MS (Ascherio & Munger, 2007).

COVID-19 Vaccination and Autoimmune Responses

Vaccination, including those against viral infections like influenza and hepatitis B, has been historically associated with rare autoimmune responses (Agmon-Levin et al., 2009). COVID-19 vaccines, particularly the mRNA vaccines developed by Pfizer-BioNTech and Moderna, have been the subject of intense study due to their novel mechanism of action (Polack et al., 2020).

While the vast majority of vaccinated individuals have experienced no serious side effects, there have been isolated reports of autoimmune diseases manifesting after COVID-19 vaccination (Mehrotra et al., 2021). These include conditions such as Guillain-Barré syndrome, myocarditis, and in rare cases, MS-like symptoms. However, a 2021 study reported an increase in autoimmune conditions following COVID-19 vaccination, though causality was not established (Baker et al., 2021). Another study from 2022 evaluated the onset of demyelinating diseases post-vaccination and concluded that, while there were isolated cases of MS, the overall risk remained extremely low, suggesting no significant elevation compared to the general population (Wingerchuk et al., 2022).

Pediatric and Adolescent MS Post-COVID-19 Vaccination

Though MS predominantly affects adults, cases in pediatric and adolescent populations have been documented, though they account for less than 10% of total MS cases (Chitnis, 2013). The onset of MS in children and adolescents following COVID-19 vaccination has been particularly rare, with only a handful of cases reported globally (Brum et al., 2022). These cases raise questions about whether vaccination could act as a trigger for MS in younger populations or if these occurrences are coincidental. Studies focusing on pediatric post-vaccination MS have shown that the disease's progression may differ slightly in younger patients compared to adults (Brum et al., 2022). The immune response to vaccines in children is typically more robust, which has led to speculation about whether this heightened immune activity could play a role in triggering autoimmune conditions like MS in susceptible individuals.

The Immune Mechanisms Behind MS Onset Post-Vaccination

Theories on the relationship between vaccination and MS onset largely focus on molecular mimicry and the activation of latent autoimmune conditions. Molecular mimicry occurs when the immune system confuses vaccine antigens with host proteins, leading to an autoimmune response (Wraith, Goldman, &

Lambert, 2003). In the case of COVID-19 vaccines, the spike protein of the virus has been suggested as a potential trigger for such responses, although no conclusive evidence has been found to confirm this mechanism (Wingerchuk et al., 2022).

Other proposed mechanisms include the reactivation of latent viruses, such as EBV, in response to vaccination, which may lead to the development or acceleration of autoimmune conditions like MS (Brum et al., 2022). Some researchers argue that individuals with a genetic predisposition to MS could be more vulnerable to post-vaccination autoimmune reactions, though more research is needed to clarify these relationships.

Refutations and Counterarguments

Despite the reported cases of MS following COVID-19 vaccination, there is significant evidence suggesting that these occurrences may be coincidental rather than causal. One of the strongest counterarguments is that MS has a baseline incidence rate that remains consistent across populations, irrespective of vaccination (Baker et al., 2021). Furthermore, large-scale epidemiological studies have found no statistically significant increase in MS diagnoses post-vaccination compared to the general population's risk of developing the disease (Wingerchuk et al., 2022).

Additionally, MS is a disease with a complex and multifactorial etiology, and attributing its onset to a singular event, such as vaccination, oversimplifies its pathogenesis (Dendrou et al., 2015). Many of the reported cases may be due to the natural progression of the disease in individuals who were already predisposed to developing MS, rather than being directly caused by the vaccine (Brum et al., 2022).

Given the relatively low number of reported MS cases post-vaccination and the extensive safety data from vaccine trials, it is likely that the benefits of COVID-19 vaccination in preventing severe illness outweigh the risks of potential autoimmune responses, particularly when the risk of MS onset remains exceedingly low (Polack et al., 2020).

METHODOLOGY

This study employs a retrospective cohort analysis, utilizing data from publicly available registries and clinical reports to assess the incidence of Multiple Sclerosis (MS) after COVID-19 vaccination. A comprehensive review of case reports and epidemiological studies was conducted, focusing on individuals who were diagnosed with MS within six months of receiving a COVID-19 vaccine.

Data Sources

The data for this study was extracted from:

- The Vaccine Adverse Event Reporting System (VAERS) for post-vaccination adverse events.
- Peer-reviewed articles from databases such as PubMed, Scopus, and Web of Science.
- National MS registries and hospital records where COVID-19 vaccination status was available.

Study Population

The study included:

- Adults (≥18 years old), adolescents (12-17 years old), and children (<12 years old) who received a COVID-19 vaccine between December 2020 and July 2023.
- The primary outcome was the onset of clinically confirmed MS, defined by the 2017 McDonald criteria (Thompson et al., 2018).
- The study analyzed data from 450 vaccinated individuals who developed MS and compared these to a control group of 3,000 vaccinated individuals without MS onset. These controls were matched by age, gender, and vaccine type.

Statistical Analysis

Incidence rates of MS in the vaccinated population were calculated per 100,000 individuals. Statistical significance was determined using the chi-square test, with a p-value of <0.05 considered significant. The relative risk (RR) of developing MS post-vaccination was calculated, alongside a 95% confidence interval (CI) to assess the association strength.

RESULTS

Incidence of Multiple Sclerosis Post-Vaccination

Across the study population, 450 individuals developed MS within six months of receiving a COVID-19 vaccine. The overall incidence of MS among vaccinated individuals was calculated at approximately

15 cases per 100,000 vaccinated individuals.

- Adults: The incidence rate of MS in vaccinated adults was 20 per 100,000 individuals.
- Adolescents (12-17 years): The incidence rate was lower, at 7 per 100,000 individuals.
- Children (<12 years): The incidence rate was the lowest, at 3 per 100,000 individuals.

The baseline incidence of MS in the general population (not vaccinated) is approximately 10 per 100,000 individuals annually (Compston & Coles, 2008). Thus, the incidence in adults post-vaccination represents a small but statistically significant increase (p=0.03), particularly when compared to the general population.

Relative Risk Analysis

The relative risk (RR) of developing MS after vaccination was calculated as follows:

- Adults: RR = 1.35 (95% CI: 1.12-1.60)
- Adolescents: RR = 0.70 (95% CI: 0.45-1.05)
- Children: RR = 0.30 (95% CI: 0.12-0.72)

These results indicate a modest increase in the relative risk of MS among vaccinated adults, while no significant increased risk was observed in adolescents and children.

Comparison of Vaccine Types

Of the 450 cases of MS, 350 cases (78%) occurred in individuals who received mRNA-based vaccines (Pfizer-BioNTech or Moderna), while the remaining 100 cases (22%) were among those who received viral vector vaccines (AstraZeneca or Johnson & Johnson). The incidence rates for MS were slightly higher among individuals vaccinated with mRNA vaccines, though this difference was not statistically significant (p=0.08).

Demographic Analysis of MS Cases Post-COVID-19 Vaccination

To provide a clearer understanding of the relationship between COVID-19 vaccination and MS onset, the 450 identified cases were analyzed by demographic characteristics such as age, sex, and type of vaccine received. This section provides a detailed breakdown of the data to help identify any patterns or specific groups that may be more at risk.

Detailed Breakdown of MS Cases by Age and Sex

Children (<12 Years)

- Number of Cases: 30
- Sex Distribution:
  - Male: 12 (40%)
  - Female: 18 (60%)
- Vaccine Distribution:
  - Pfizer-BioNTech: 16 cases (53.3%)
  - Moderna: 9 cases (30%)
  - AstraZeneca: 3 cases (10%)
  - Johnson & Johnson: 2 cases (6.7%)

Adolescents (12-17 Years)

- Number of Cases: 35
- Sex Distribution:
  - Male: 14 (40%)
  - Female: 21 (60%)
- Vaccine Distribution:
  - Pfizer-BioNTech: 20 cases (57.1%)
  - Moderna: 10 cases (28.6%)
  - AstraZeneca: 3 cases (8.6%)
  - Johnson & Johnson: 2 cases (5.7%)

Adults (18-40 Years)

- Number of Cases: 190
- Sex Distribution:
  - Male: 65 (34.2%)
  - Female: 125 (65.8%)
- Vaccine Distribution:
  - Pfizer-BioNTech: 105 cases (55.3%)

- Moderna: 50 cases (26.3%)
- AstraZeneca: 20 cases (10.5%)
- Johnson & Johnson: 15 cases (7.9%)

Adults (41-60 Years)

- Number of Cases: 130
- Sex Distribution:
  - Male: 45 (34.6%)
  - Female: 85 (65.4%)
- Vaccine Distribution:
  - Pfizer-BioNTech: 70 cases (53.8%)
  - Moderna: 25 cases (19.2%)
  - AstraZeneca: 20 cases (15.4%)
  - Johnson & Johnson: 15 cases (11.5%)

Adults (>60 Years)

- Number of Cases: 65
- Sex Distribution:
  - Male: 29 (44.6%)
  - Female: 36 (55.4%)
- Vaccine Distribution:
  - Pfizer-BioNTech: 34 cases (52.3%)
  - Moderna: 11 cases (16.9%)
  - AstraZeneca: 9 cases (13.8%)
  - Johnson & Johnson: 11 cases (16.9%)

Consolidated Statistical Observations

Age: The most affected age group is adults aged 18-40 years (42.2% of total cases), with children under 12 years experiencing the lowest incidence rate of MS post-vaccination (6.7% of total cases).

Sex: Females are disproportionately affected, representing 63.3% of all cases. The female-to-male ratio is approximately 1.7:1, which is consistent with global MS patterns.

Vaccine Type: The majority of MS cases post-vaccination are linked to the Pfizer-BioNTech vaccine (54.4% of cases), though this may be reflective of its wider usage globally. Moderna accounts for 23.3%, while AstraZeneca and Johnson & Johnson vaccines account for smaller proportions (12.2% and 10%, respectively).

DISCUSSION OF FINDINGS

The analysis reveals patterns consistent with established MS epidemiology, particularly in terms of age and sex distribution. The female predominance and higher incidence in younger adults support the notion that individuals in these categories may have an underlying predisposition to MS, which could be triggered by an environmental factor such as vaccination.

However, it is important to emphasize that despite the higher number of cases associated with specific vaccines, the absolute risk of developing MS post-vaccination remains extremely low. Additionally, no significant increase in risk was observed in children or adolescents, reinforcing the safety of COVID-19 vaccination in these populations.

Future studies should aim to further dissect the potential mechanisms that may explain why some individuals develop MS post-vaccination, particularly those involving immune responses or latent viral reactivation.

The results of this study suggest a small but noticeable increase in the incidence of MS among adults following COVID-19 vaccination, particularly for those who received mRNA-based vaccines. However, the incidence rates in adolescents and children did not exhibit a similar pattern, suggesting that younger populations may be less susceptible to vaccine-related autoimmune triggers.

Explaining the Adult Risk Increase

One possible explanation for the increased incidence in adults may be related to the natural course of MS in this age group. MS often has an onset in early adulthood, and the temporal association with vaccination could be coincidental rather than causal. However, the modestly elevated risk in adults (RR = 1.35) raises the possibility that vaccination may, in some cases, act as a trigger in individuals predisposed to MS.

Another explanation involves the immune response elicited by mRNA vaccines, which may, in rare cases, activate latent autoimmune processes (Wingerchuk et al., 2022). Despite this, the absolute

increase in risk remains small, and the benefits of vaccination against severe COVID-19 far outweigh the risks of potential autoimmune complications.

Limitations of the Study

This study has several limitations. First, the data used is retrospective, relying on reported cases of MS and therefore may suffer from underreporting or misclassification. Additionally, the observational nature of the study limits the ability to establish a definitive causal relationship between vaccination and MS onset. Another limitation is the potential for confounding factors, such as undiagnosed MS prior to vaccination or viral triggers unrelated to the vaccine.

Counterarguments and Refutations

Critics may argue that the temporal relationship between vaccination and MS onset is not sufficient to prove causality, especially given that MS can take years to manifest clinically. The incidence rates observed in vaccinated individuals may simply reflect the natural variability of MS diagnosis within the population. Furthermore, large-scale studies have found no significant increase in MS risk among vaccinated individuals compared to unvaccinated groups, particularly when adjusting for confounders such as prior viral infections and genetic susceptibility (Baker et al., 2021).

Age Distribution of MS Cases Post-Vaccination

Age Group	Number of MS Cases	Percentage of Total Cases (%)	Incidence per 100,000 Vaccinated
Children (<12)	30	6.7%	3 per 100,000
Adolescents (12-17)	35	7.8%	7 per 100,000
Adults (18-40)	190	42.2%	18 per 100,000
Adults (41-60)	130	28.9%	22 per 100,000
Adults (>60)	65	14.4%	16 per 100,000
Total	450	100%	15 er 100,000

Analysis: The majority of cases (42.2%) were observed in young to middle-aged adults (18-40 years), aligning with the known age of peak onset for MS. The incidence rates suggest that the risk of MS post-

vaccination is highest in adults between the ages of 41 and 60 years, followed by younger adults aged 18-40 years.

Sex Distribution of MS Cases Post-Vaccination

Sex	Number of MS Cases	Percentage of Total Cases (%)	Incidence per 100,000 Vaccinated
Male	165	36.7%	12 per 100,000
Female	285	63.3%	18 er 100,000

Analysis: MS cases post-vaccination were more prevalent among females (63.3%) compared to males (36.7%), consistent with the general trend observed in MS epidemiology, where females are at a higher risk of developing the disease. The incidence rate for females was also higher at 18 per 100,000, compared to 12 per 100,000 for males.

Vaccine Type and MS Cases Post-Vaccination

Vaccine Type	Number of MS Cases	Percentage of Total Cases (%)	Incidence per 100,000 Vaccinated
Pfizer-BioNTech	245	54.4%	16 per 100,000
Moderna	105	23.3%	15 per 100,000
AstraZeneca	55	12.2%	11 per 100,000
Johnson & Johnson	45	10.0%	9 per 100,000

Analysis: The majority of cases occurred in individuals vaccinated with Pfizer-BioNTech (54.4%), followed by Moderna (23.3%). Despite the higher proportion of cases associated with mRNA vaccines, the differences in incidence rates among the different vaccines were not statistically significant (p=0.08). It is important to note that the overall risk remains very low across all vaccine types.

CONCLUSIONS

This study highlights the importance of ongoing surveillance and careful monitoring of autoimmune conditions following COVID-19 vaccination. While the data suggests a small increase in MS incidence among adults post-vaccination, this risk remains low, particularly when considering the overwhelming public health benefits of COVID-19 vaccines. In younger populations, no significant increased risk of

MS was observed.

Further research is warranted to better understand the potential mechanisms behind vaccine-related autoimmune triggers and to identify populations that may be at greater risk. Ultimately, the findings support the continued use of COVID-19 vaccines, emphasizing their safety and efficacy for the vast majority of individuals.

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