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REVIEW

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The heart versus the brain, are they also different when it comes to post-vaccination complications, insights from a systematic review of post-COVID-19 vaccines ADEM cases

Antoine AbdelMassih[1,2*], Aya Kamel[3], Ameera Barakat[4], Lana Mohammad[4], Hanya Gaber[5], Yasmine Hisham Mousa[5], Hana Hassanein[6], Robert Saleb[5] and Noha Khalil[7]

Abstract

Background COVID-19 vaccines have been a game changer in the pandemic, their extensive use was favorable compared to the burden of COVID-19 complications. Despite the low incidence of complications, it was important to analyze them carefully to understand the underlying mechanisms and predisposing factors. For instance, myopericarditis especially from mRNA vaccines, and its relatively higher prevalence in young adults and adolescents has raised a public concern about the use of this vaccine in this group. We aimed through this review to compare the age likelihood of ADEM from COVID-19 vaccines, with that reported in myopericarditis cases; secondary outcome parameters included the gender and number of doses needed to induce COVID-19 vaccines related to ADEM.

Methodology A literature search has been conducted on relevant databases to retrieve all case reports/series and systematic reviews describing ADEM with possible linkage to COVID-19. Exclusion criteria included any report not including the desired outcome parameters. Our results were then qualitatively compared with a similar systematic review reporting myopericarditis from COVID-19 vaccines.

Results In 38 cases with ADEM, mean age was 49 ± 16 compared to 25 ± 14 in myopericarditis, females were more likely to be affected, and while most of myopericarditis cases develop after the second dose, most of ADEM cases develop after the first dose (76%). Moreover, age > 56 years was more predictive of negative outcome after ADEM in the form of death or permanent vegetative state.

Short conclusion The discrepancy in age, gender and number of doses needed to induce complications between ADEM and myopericarditis, signify that the tissue affected is the major orchestrator of the age, gender, and dose characteristics, and not the type of vaccines. A leakier blood brain barrier with aging, might allow easier passage of autoantibodies and cytokines into the brain while lack of inhibitory immune checkpoints in the myocardium in young age might explain the higher prevalence of those cases in young adults and adolescents.

Keywords COVID-19 vaccines, ADEM, Myopericarditis

*Correspondence:
Antoine AbdelMassih
antoine.abdelmassih@kasralainy.edu.eg
Full list of author information is available at the end of the article

Background

There has been a dilemma in the diversified sequelae of post-COVID-19 (coronavirus disease 2019) mRNA (messenger Ribonucleic acid) vaccinations. Although most of the outcomes are satisfactory, and vaccination benefits outweighs the risk, there have been some case reports that intrigued further analysis. A study conducted by *Minghui Li* et al. assessed the incidence rate of myocarditis and pericarditis following COVID-19 vaccination in the USA in perspective to age group and vaccine type (Li et al. 2021). It was found that the rates of myocardial affection are more prevalent in adolescents and young adults than in older age groups while using the mRNA vaccines. As the reporting odds ratio (ROR) of BNT162b2 (Pfizer-Biontech) and mRNA-1273 (Moderna) vaccine subtypes were higher than the ROR of viral vector vaccines of Ad26.COV2. S (Janssen), 5.3, 2.91 and 1.39, respectively. Another study supports the outcomes of mRNA vaccination post-COVID-19 in youths. A retrospective study was implemented by *Dongngan T. Truong* et al., and the results of the collected data on patients < 21 years old following mRNA vaccination were significant. (Truong et al. 2022) The incidence of suspected myocarditis in younger patients was noticeable.

The affection of young age by postvaccine myocarditis has not only be observed with mRNA vaccines; as myocardial and pericardial complications can also occur in young age groups following the smallpox vaccine, not only after the COVID-19 mRNA vaccine. This can be supported by an observational cohort study conducted by *Engler* et al., where the outcomes of smallpox vaccines were elaborated (Engler et al. 2015). Three hundred and forty-eight individuals out of over 5000 case reports that showed side effects post smallpox vaccination, manifested with cardiological adversities such as myocarditis and pericarditis: 276 and 72 cases, respectively. The median age of the myopericarditis cases was 24 years old, emphasizing the prevalence of myocarditis post-vaccination in the younger segment of the age spectrum, irrespective to vaccination subtype.

This young age trend for postvaccine myocarditis, regardless of the type of vaccine, is poorly understood.

In contrast, postvaccine acute disseminated encephalomyelitis (ADEM), tend to occur in a relatively older age. A report by Huynh and colleagues illustrated a case of 61-year-old male with ADEM following influenza vaccine, while Nakamura et al. documented two adult cases aged 62 and 70 with post-influenza vaccine ADEM (Huynh et al. 2008; NAKAMURA et al. 2003). The rest of systematic reviews were mainly focused on postvaccine neurologic sequelae overall and not specifically targeting the specific age of ADEM following different types of vaccines. In addition most of the studies assessing postvaccine ADEM, cannot be reliably cited as the involved vaccines are exclusive childhood compulsory vaccines, thus they cannot reflect the true age trend of postvaccine ADEM. (Sejvar 2005; Williams et al. 2011).

It seems, from the above that age likelihood of postvaccine tissue affection, might be related to the tissue characteristics rather than to the vaccine type. For this purpose, we dedicate this systematic review, to study the age likelihood of acute disseminated encephalomyelitis (ADEM), post-COVID-19 vaccination specifically post-mRNA COVID-19 vaccines. We hypothesize that we might find a discrepancy between the mean age of ADEM cases reported after COVID-19 vaccines compared to myocarditis seen after the same vaccines. The latter finding might consolidate our initial impression that tissue characteristics might be closely tied to the age predilection of post-vaccination immune sequelae in the respective tissue.

Methodology

Inclusion and exclusion criteria for literature search

A literature search was implemented on PubMed, Scopus, Google scholar and Web of science to identify studies using the following key words ADEM **and** COVID-19 vaccination. The bibliography of any identified study was clearly inspected to find any report that could have been missed during the initial computer run.

Inclusion criteria included any age, developing ADEM after COVID-19 vaccination, accepted type of studies were systematic reviews, case reports, and case series.

Studies not fulfilling the outcome parameters targeted by the study were excluded.

Outcome parameters

Three of the authors examined each study for the following outcome parameters: age, gender, type, and dose of the vaccine incriminated, the time interval between the vaccination and the development of ADEM, the main neurologic presentation, the treatment lines used, and the outcome of the case.

Statistical analysis

Data collected were analyzed using Excel and MedCalc statistical software. Numerical data were represented using mean and standard deviation when normally distributed and using median, minimum, and maximum when non-normally distributed. Non-recovery was defined as persistence of neurologic abnormalities, vegetative state or death in our collected cases, this categorical division was essential to perform a Receiver Operating Characteristic analysis (ROC) to determine the cut-off age predicting non-recovery from ADEM

developing from COVID-19 vaccines. The latter was represented using an interactive dot diagram.

Results

A systematic review has been identified (Nabizadeh et al. 2023) including 20 studies, out of which 19 were eligible to be included in our review: (Ahmad, Timmermans, and Dakakni 2022; Al-Quliti et al. 2022; Ancau et al. 2022; Ballout et al. 2022; Cao and Ren 2022; Kania et al. 2021; Lazaro et al. 2022; Maramattom et al. 2022; Miyamoto et al. 2022; Mumoli et al. 2022; Nagaratnam et al. 2022; Netravathi et al. 2022; Ozgen Kenangil et al. 2021; Permezel et al. 2022; Rinaldi et al. 2022; Shimizu et al. 2021; Simone et al. 2021; Vogrig et al. 2021; Yazdanpanah et al. 2022) (Fig. 1).

In addition to the 19 studies included, our literature search has identified nine other studies:

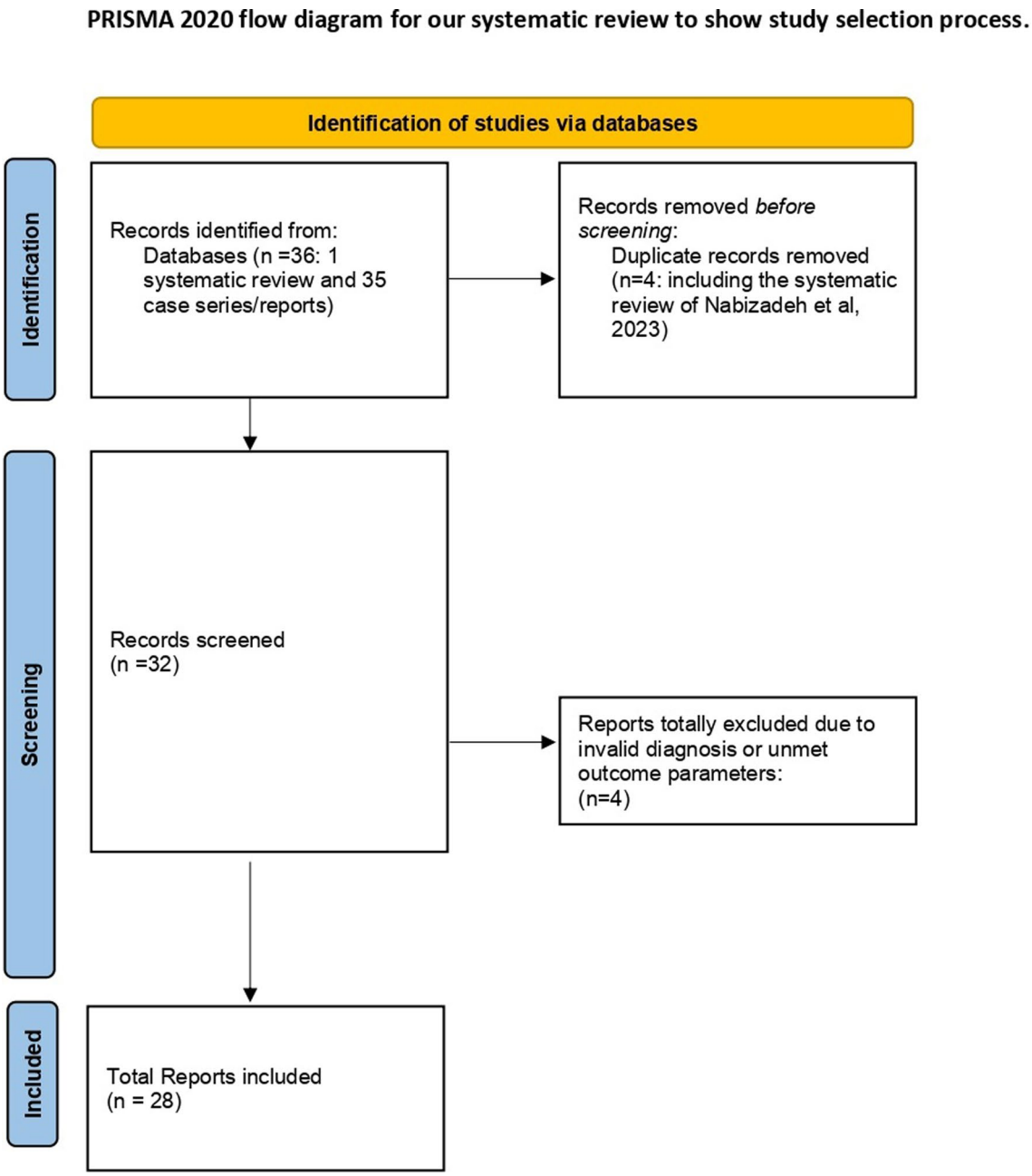

Fig. 1 PRISMA flow chart

(Bastide et al. 2022; Garg et al. 2023; Gustavsen et al. 2023; Lohmann et al. 2022; Mousa et al. 2022; Nimkar et al. 2022; Raknuzzaman 2021; Sazgarnejad and Kordipour 2022). Thus, a total of 28 studies were analyzed comprising a total of 38 cases. (Table 1).

Most of the cases were attributed to the adenoviral vector vaccines (63%) ADEM occurred following the first dose of vaccination (76%), with a median interval of 14 after vaccination. (Table 2).

The oldest age seen in ADEM cases following vaccination was seen in patients receiving mRNA vaccines (57 ± 19) compared to a mean of 48 ± 14 following adenoviral vector vaccines.

Complete recovery was observed in 37% of patients, while non-recovery (defined as residual motor deficit or the development of vegetative state) or death was observed in a total of 45% of cases. (Table 2).

Receiver operating characteristic analysis illustrated as an interactive dot diagram showed that an age > 56, predicts non-recovery in ADEM cases following post-COVID-19 vaccines. (Fig. 2).

Treatment received was mainly steroids (oral and pulse intravenous), intravenous immunoglobulins, and plasma exchange. While only three cases received rituximab (8%), and one received eculizumab and another one received cyclophosphamide (3%) (Table 1). Table 1 illustrates the details of each case in the included cases and case reports.

Discussion

Our review describes the demographic, and clinical characteristics of a rare complication of COVID-19 vaccines. It is the second systematic review of reported cases in this context, after Nabizadeh et al. study(Nabizadeh et al. 2023), however with a different aim. The aim of our systematic review was mainly to study the differences of age predisposition, type of vaccine and number of doses between myocarditis and ADEM following COVID-19 vaccines. Several major differences were observed, notably the number of literature reports, which points to a relatively higher incidence of myocarditis as our group could only find 28 reports with a total of 38 cases compared to thousands of cases of myopericarditis in the literature; this can make the comparison between the two complications flawful, as the scarcity of ADEM reports is not very helpful to draw solid conclusions.

However, we still decided to compare the aforementioned outcome parameters across the two complications. We took Goyal et al. study as a reference for myopericarditis cases as it shares the different outcome parameters intended in our study, and it is not a VAERS based study; thus, its results can be qualitatively compared to the results of our research. (Goyal et al. 2023).

Age of clustered ADEM cases was 49 ± 16 compared to 25 ± 14 in myopericarditis cases. The young age of myopericarditis especially from mRNA vaccines, lead to fears among parents, planning to vaccinate their children using these vaccines, and led to an overall impression that mRNA vaccines might be associated with increased complications' rate at the young age. Our study contradicts this false belief, as it clearly shows that ADEM occurring from mRNA vaccines is likely to occur in older age groups compared to myocarditis and to ADEM cases from other COVID-19 vaccines. Nevertheless, older age was also predictive of worst outcomes in our collected cases (Fig. 2), patients older than 56 were more prone to develop residual neurologic deficit, vegetative state, or death. This might also mean that age likelihood and other demographic characteristics of any vaccine complication are related to the type of the complication and tissue involved rather than the vaccine type.

One of the theories that can explain the young age of myocarditis from COVID-19 and other vaccines (such as vaccinia virus vaccine used for smallpox) is the mechanism of immune inhibition inside the myocardium. The heart muscle harbors a strict system for immune surveillance, that can prevent any immune-mediated damage, this immune surveillance is particularly important in the heart as the regenerative capacity of myocardial cells is absent.

Two main mechanisms of peripheral tolerance protect myocytes from T cell damage namely cytotoxic T-lymphocyte-associated protein-4 (CTLA4), and Programmed cell protein death-1 (PD1). CTLA4 and PD1 block T cell activation by binding to CD-28 receptors on the surface of T cells, thereby preventing any viral antigen from its activation. (Grabie et al. 2019) The myocardial protection from autoimmunity, offered by inhibitory immune checkpoints, such as PD1, is upregulated by aging, which might mean that the susceptibility of myocardium to immune-mediated inflammation, should decrease with aging. (Platt et al. 2017) On another note, antibodies implicated in CNS autoimmune inflammation, must gain access to the CNS via the blood brain barrier, olfactory route, or blood-cerebrospinal fluid barrier, or sometimes produced locally witing the CNS itself. The latter mechanism has been particularly of focus in multiple sclerosis, as Quintana and colleagues proved the present of myelin reactive antibodies that are locally produced in the brain. There also hypotheses that post-infectious ADEM, which is intriguingly common in the pediatric age group, involves the local production of antibodies in the CNS against viral antigen entering the CNS through the olfactory route. But, for antibodies, to gain access to the CNS, this implies a leakier BBB Blood brain barrier) or BCSFB (Blood cerebrospinal fluid barrier),

Table 1 Details of the included cases

Report	Age	Main Vaccine mechanism	Subtype of vaccine	The interval between vaccine and sequelae (days)	Dose Number	Gender	Clinical Picture	Treatment received	Recovery/Residual lesion
Raknuzzaman (2021)	55	1	mRNA (unspecified subtype)	21	NR	2	Headache, somnolence, fluctuating alertness, and orientation consistent with delirium and convulsions	MP then oral steroids	full recovery
Mousa et al. (2022)	44	1	mRNA (unspecified subtype)	6	1	1	Blurred vision, DCL, lower limb weakness, impaired sensation, urine retention	IV, oral steroids and plasmapheresis	Bilateral optic atrophy
Shimizu et al. (2021)	88	1	BNT162b2	29	2	1	impaired consciousness and gaze-evoked nystagmus	Improved on pulse IV methylprednisolone for 3 days	Progressive improvement on day 31 and day 66
Kits et al. (2022)	53	1	BNT162b2	2	2	2	Confusion and unconsciousness (GCS of 7), agitation, snoring, anisocoria, and reduced voluntary movements in the left arm and leg	MP, IVIG, PP	Remained in vegetative state
Ahmad, Timmermans, and Dakakni (2022)	61	1	BNT162b2	70	1	1	Generalized weakness and altered mental status	steroids and IVIG	Required tracheostomy and gastrostomy tube due to generalized weakness
Miyamoto et al. (2022)	54	1	BNT162b2	12	2	1	Fever, urine retention, headache, DCL, facial palsy	MP, IVIG, PP	Well recovered
Lohmann et al. (2022)	68	1	BNT162b2	23	1	1	Exacerbating of preexisting paraparesis	Improved on IV steroids and plasmapheresis. Also received eculizumab	Residual paraparesis
Vogrig et al. (2021)	56	1	BNT162b2	14	1	1	unsteadiness of gait, predominantly on the left side, followed by clumsiness of left arm	Steroids	Improvement in gait stability, being able to walk without aid. Mild dysmetria and intention tremor of the left upper limb were still present
Kania et al. (2021)	19	1	mRNA-1273	14	1	1	Severe headache, fever (37.5 °C), back and neck pain, nausea and vomiting and urinary retention	MP	Residual mild headache

Table 1 (continued)

Report	Age	Main Vaccine mechanism	Subtype of vaccine	The interval between vaccine and sequelae (days)	Dose Number	Gender	Clinical Picture	Treatment received	Recovery/Residual lesion
Ballout et al. (2022)	81	1	mRNA-1273	13	1	2	Coma	MP, IVIG, PP	Death
Garg et al. (2023)	67	2	ChAdOX1 nCoV-19	14	nr	1	symptoms of encephalopathy	The patient was given steroids, and a good response was reported	good response was reported
Nimkar et al. (2022)	77	2	ChAdOx1 nCov-19	15	1	1	Altered sensorium for four hours, aphasia for four hours, and loss of consciousness within one hour. Altered mental status for 15 days	MP	vegetative state
Bastide et al. (2022)	49	2	ChAdOx1 nCoV-19	7	1	1	flu-like symptoms with fever, fatigue, neck pain, paraesthesia in both legs, up to the chest, Lhermitte's phenomenon and sphincter dysfunction	MP then readmission/ PP, rituximab	3 relapses, residual paraparesis
Nagaratnam et al. (2022)	36	2	ChAdOx1 nCoV-19	14	1	1	Reduced visual acuity, headache, fatigue, painful eye movement	Significant improvement on IV and oral steroids	Mild impairment of visual acuity, one relapse
Maramattom et al. (2022)	64	2	ChAdOx1 nCoV-19	20	2	2	leg stiffness hand parathesia	IVIG	Mild residual paresis
	46	2	ChAdOx1 nCoV-19	4	1	2	LL weakness	IVIG, MP	Improvement
	42	2	ChAdOx1 nCoV-19	5	1	1	headache/photophobia		spontaneous improvement
Al-Quliti et al. (2022)	56	2	ChAdOx1 nCoV-19	10	1	1	LL weakness	MP	Complete resolution
Ancau et al. (2022)	61	2	ChAdOx1 nCoV-19	2	1	2	Coma	MP	vegetative state
	25	2	ChAdOx1 nCoV-19	9	1	1	Ascending weakness and numbness	MP/plasma exchange	Persistent hemiplegia
	55	2	ChAdOx1 nCoV-19	9	1	1	Tetraparesis	Steroids	Death
Mumoli et al. (2022)	45	2	ChAdOx1 nCoV-19	7	1	2	Paraparesis and urine retention	MP	Persistence of urine retention
Rinaldi et al. (2022)	45	2	ChAdOx1 nCoV-19	12	1	2	Numbness, decreased visual acuity	–	Complete recovery
Permezel et al. (2022)	63	2	ChAdOx1 nCoV-19	12	1	2	Coma	MP-PP	Death

Table 1 (continued)

Report	Age	Main Vaccine mechanism	Subtype of vaccine	The interval between vaccine and sequelae (days)	Dose Number	Gender	Clinical Picture	Treatment received	Recovery/Residual lesion
Netravathi et al. (2022)	54	2	ChAdOx1 nCoV-19	14	1	1	Quadriparesis	MP + PP	NR
	35	2	ChAdOx1 nCoV-19	9	1	1	Paraparesis and sensory disturbances	MP	NR
	33	2	ChAdOx1 nCoV-19	14	1	1	Persistent sensory disturbances below midthoracic level	MP + PP	NR
	60	2	ChAdOx1 nCoV-19	14	2	2	Sensory disturbances, left hemiparesis, memory and behavior disturbances	MP	NR
	45	2	ChAdOx1 nCoV-19	10	1	2	Urine retention, altered sensorium	MP + PP	NR
	52	2	ChAdOx1 nCoV-19	35	1	1	Slurred speech, swallowing difficulties, paresis involving right side	MP + rituximab	NR
	20	2	ChAdOx1 nCoV-19 of the COVAX initiative	1	1	1	Paraparesis and altered sensorium	MP + PP	NR
Gustavsen et al. (2023)	31	2	Ad26.COV2	28	1	1	right-sided weakness and numbness during a three-week period	MP	complete clinical recovery at the four-month follow-up
Lazaro et al. (2022)	26	2	*Gam*-COVID-Vac (sputnik)	28	1	1	Disorientation/gait imbalance	MP	Complete resolution
Simone et al. (2021)	51	2	Adenoviral vector vaccine (unspecified)	-	nr	1	Paraparesis and urine retention	MP,	Improved
Sazgarnejad and Kordipour (2022)	45	3	BBIBP-CorV	28	1	2	Acute disorientation and fever	No significant improvement on pulse corticosteroids and plasmapheresis. Also received cyclophosphamide and rituximab	Residual aphasia and paresis
Cao and Ren (2022)	24	3	BBIBP-CorV	14	1	1	Memory decline	IVIG	Complete resolution
Yazdanpanah et al. (2022)	37	3	BBIBP-CorV	30	1	2	Tetraparesis	MP + PP	Improvement of motor function

Table 1 (continued)

Report	Age	Main Vaccine mechanism	Subtype of vaccine	The interval between vaccine and sequelae (days)	Dose Number	Gender	Clinical Picture	Treatment received	Recovery/Residual lesion
Ozgen Kenangil et al. (2021)	46	3	CoronaVac	30	2	1	Seizure	Steroids	Persistence of abnormal MRI

Ad26.COV2 Janssen vaccine, *BBIBP-CorV* Sinopharm, *BNT162b2* Pfizer Biontech vaccine, *CoronaVac* Sinovac, *ChAdOx1 nCoV-19* Chimpanzee (Ch) adenovirus-vectored vaccine (Ad), whose development was led by the University of Oxford (Ox), Gam-COVID-Vac*Gam* Gamaleya, COVID-Sputnik Vaccine, *IVIG* Intravenous immunoglobulins, *IV* intravenous, *LL* Lower limb, *MRI* magnetic resonance imaging, *MP* Methylprednisone, *NR* Not reported, *PP* Plasmapheresis

Table 2 Summary statistics of ADEM developing following COVID-19

Age in patients receiving mRNA vaccines. Mean ± SD	**57 ± 19**
Age in patients receiving adenoviral vaccines. Mean ± SD	48 ± 14
Age in patients receiving inactivated vaccines. Mean ± SD	38 ± 10
Age in overall patients Mean ± SD	49 ± 16
Sex distribution in the collected cases *n* (%)	Female 25(66)
	Male 13(34)
Major vaccine type distribution in the collected cases *n* (%)	mRNA 10(26)
	Adenoviral vector 24 (63)
	Inactivated 4 (11)
Dose distribution in the collected cases *n* (%)	1st dose 29 (76)
	2nd dose 6 (16)
	NR 3 (8)
Interval between vaccination and ADEM Median (min–max)	14
Major outcome of collected cases *n* (%)	Complete clinical recovery 14 (37)
	Residual Neurologic deficit 10 (26)
	Vegetative state 4 (11)
	Death 3 (8)
	NR 7 (18)

ADEM Acute disseminated encephalomyelitis, *COVID-19* Coronavirus disease, *mRNA* Messenger Ribonucleic acid, *n* number, *NR* not reported, *SD* standard deviations

this can be understandable in post-infectious ADEM, where implicated micro-organisms weaken the tight junctions of the BBB, and this allows access of cross-reactive antibodies to the brain (Spindler and Hsu 2012); but this cannot be the case in post-vaccination ADEM, as no offending organism is present to play this synergistic getaway role. An explanation for antibody access to the CNS in post-vaccination ADEM, is aging. If aging protects the myocardium against autoimmunity, it plays an inverse role in the CNS by rendering the BBB and BCSFB more permeable to antibodies and to external antigens. (Adesse et al. 2022).

Back to the findings, of our study, which also showed that ADEM mainly occurs after the first dose of vaccination, this is different than the immune-priming pattern seen in myocarditis from COVID-19 vaccines, as they need two doses usually to produce this complication.

This pattern might be consistent with a cytokine rather than immune-mediated damage. Wu et al. described a subtype of ADEM known as acute necrotizing encephalitis which involves a personal susceptibility to CNS damage due to hypercytokinemia. (Wu et al. 2015).

Finally, yet importantly female patients were more likely to develop ADEM following COVID-19 vaccination compared to male patients. A study by Falahi et al., examined COVID-19 outcomes across both genders, and showed that female patients have a higher susceptibility to cytokine storm, and suggested that estrogen upregulates pro-inflammatory molecules, leading to an augmented inflammatory response in females. This might consolidate the impression taken from dose pattern of post-COVID-19 vaccination ADEM, that it is mainly mediated via hypercytokinemia rather than auto-antibodies. (Falahi and Kenarkoohi 2021).

It is worth highlighting again as mentioned in the first paragraph of the discussion, that one of the most important limitations of this study that can hinder the solidity of our results; is the discrepancy in the number of cases across the two complications (ADEM and myopericarditis); with only 38 ADEM cases compared to hundreds of myopericarditis patients.

Figure 3 summarizes the differences outlined above between ADEM and myopericarditis developing following COVID-19 vaccines in view of our findings compared to the findings of Goyal et study (2023).

Conclusions

This review compares the demographic, vaccine types and dose characteristics of post-COVID-19 vaccines ADEM and Post-COVID-19 vaccines myopericarditis. Older age, predominance of female gender, and first dose implication all characterize ADEM compared to myopericarditis. And despite the rarity of these complications, they open new horizons in understanding post-vaccination complications and their underlying mechanisms. They might signify that aging can be protective against autoimmunity in the myocardium, but the same aging can jeopardize the BBB, rendering it more susceptible to delivery of antibodies and cytokines to the CNS. More studies at the molecular

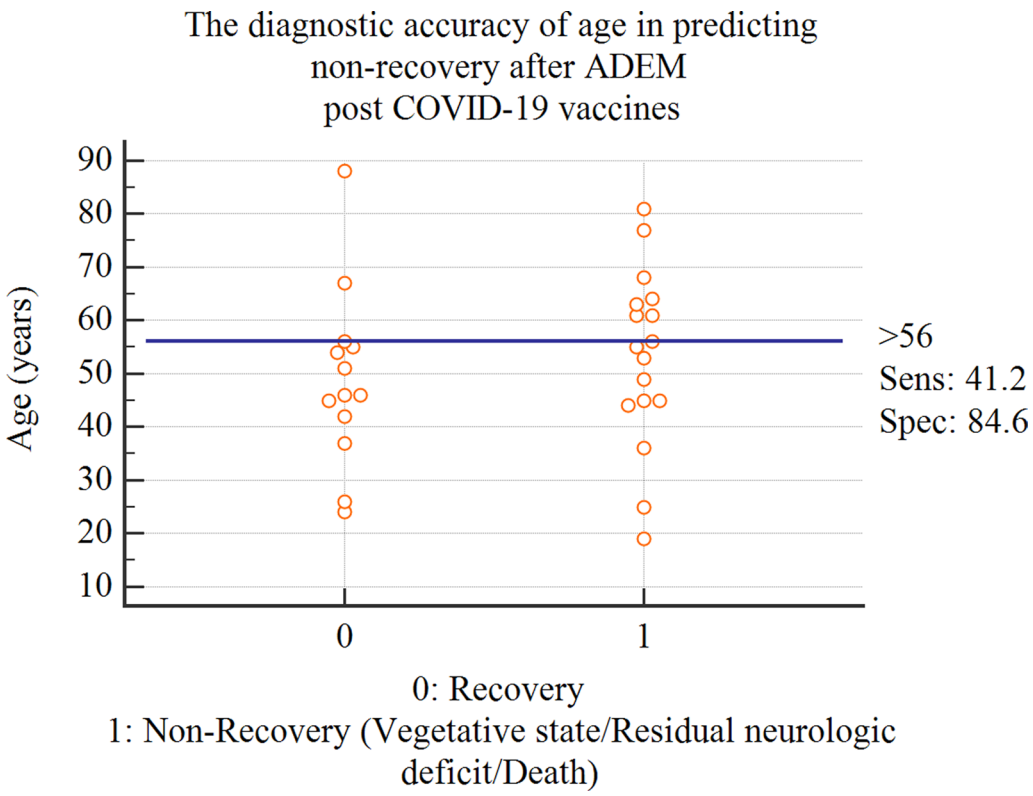

Fig. 2 The diagnostic accuracy of age in predicting non-recovery after ADEM post COVID-19 Vaccines. *ADEM* acute disseminated encephalomyelitis, *COVID-19* Coronavirus Disease 2019

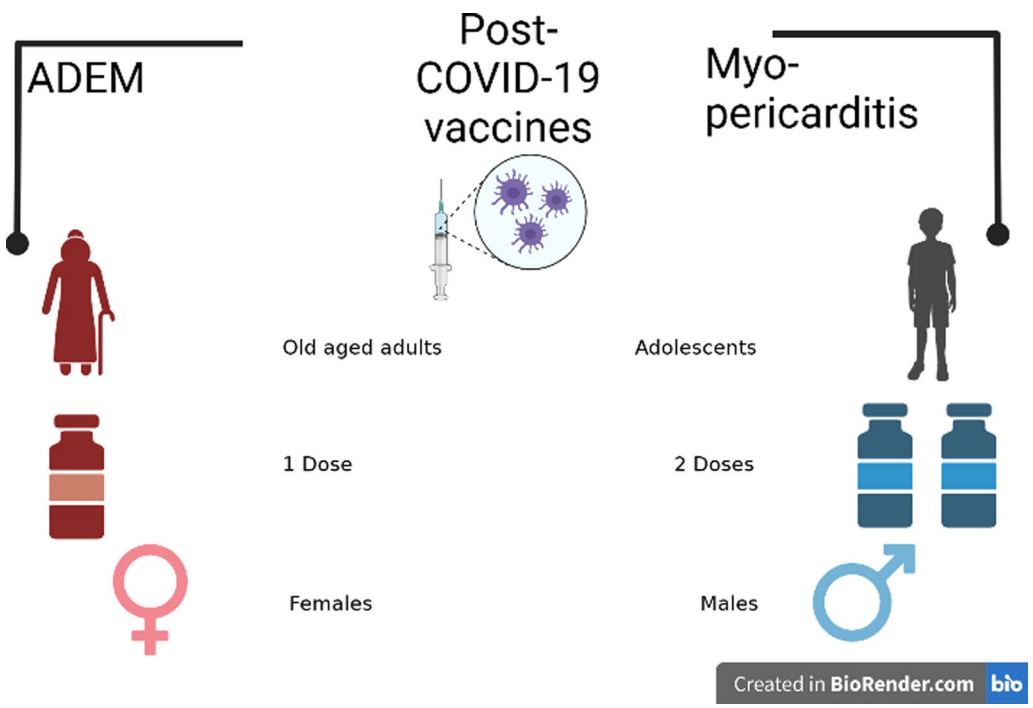

Fig. 3 Summary figure for comparison of age, sex, and dose characteristics of post COVID-19 myopericarditis vs. ADEM. ADEM: acute disseminated encephalomyelitis, COVID-19: Coronavirus Disease 2019

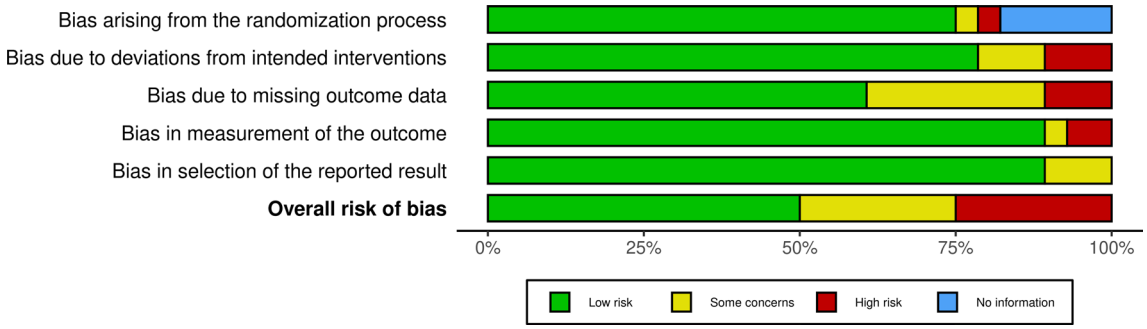

Fig. 4 Risk of bias assessment for our systematic review

level, should be implemented to confirm these findings and to prove that vaccine complications are not only determined by the vaccine type but also by the type of the target tissue. The findings highlighted by our study, can wipe out the public-based impression that mRNA vaccines are linked to higher complications in younger individuals, and can help in combating vaccine hesitancy especially toward a vaccine mechanism that might be very promising in the future for other infectious and non-infectious disorders. Risk of Bias assessment has been performed and illustrated in Fig. 4:

Abbreviations

Ad26.COV2.	Janssen vaccine
ADEM	Acute Disseminated Encephalomyelitis
BBB	Blood brain Barrier
BBIBP-CorV	Sinopharm
BCSFB	Blood cerebrospinal fluid barrier
BNT162b2	Pfizer Biontech vaccine
CD	Cluster of differentiation
ChAdOx1 nCoV-19	Is a chimpanzee (Ch) adenovirus-vectored vaccine (Ad), whose development was led by the University of Oxford (Ox).
CNS	Central nervous system
CoronaVac	Sinovac
Covax	Coronavirus vaccine initiative
COVID-19	Coronavirus Disease 2019
CTLA4	Cytotoxic T-lymphocyte-associated protein-4
DCL	Disturbed Conscious level
Gam-COVID-Vac	Gam: Gamaleya, COVID-Sputnik Vaccine
GCS	Glasgow Coma Scale
IV	Intravenous
IVIG	Intravenous immunoglobulins
LL	Lower Limb
MP	Methylprednisolone
mRNA	Messenger Ribonucleic acid
mRNA	Messenger Ribonucleic acid
mRNA-1273	Moderna Spikevax vaccine
NR	Not reported
PD-1	Programmed Death ligand 1
PP	Plasmapheresis
VAERS	Vaccine adverse events Reporting system

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Author details
[1]Department of Pediatrics, Pediatric Cardiology Unit, Cairo University Children Hospital, Cairo University, Cairo, Egypt. [2]Cardiac Sciences Department, Pediatric Cardiology Division, Sheikh Khalifa Medical City, Abu Dhabi, UAE. [3]Department of Pulmonology, Faculty of Medicine, Cairo University, Cairo, Egypt. [4]Clinical Pharmacy Department, Sheikh Khalifa Medical City, Abu Dhabi, UAE. [5]Students' and Interns' Research Program (Research Accessibility Team), Faculty of Medicine, Cairo University, Cairo, Egypt. [6]Students' and Interns' Research Program (Research Accessibility Team), Faculty of Dentistry, Cairo University, Cairo, Egypt. [7]Pediatric Residency Program, Ministry of Health, Cairo, Egypt.

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References

Adesse D et al (2022) Role of aging in blood-brain barrier dysfunction and susceptibility to SARS-CoV-2 infection: impacts on neurological symptoms of COVID-19. Fluids and Barriers of the CNS 19(1):1–19. https://doi.org/10.1186/s12987-022-00357-5

Ahmad HR, Timmermans VM, Dakakni T (2022) Acute Disseminated encephalomyelitis after SARS-CoV-2 vaccination. Am J Case Rep. https://doi.org/10.12659/AJCR.936574
Al-Quliti K et al (2022) Acute demyelinating encephalomyelitis post-COVID-19 vaccination: a case report and literature review. Diseases 10(1):13
Ancau M et al (2022) Case series: acute hemorrhagic encephalomyelitis after SARS-CoV-2 vaccination. Front Neurol. https://doi.org/10.3389/fneur.2021.820049/full
Ballout AA et al (2022) A Single-health system case series of new-onset CNS inflammatory disorders temporally associated with MRNA-based SARS-CoV-2 vaccines. Front Neurol 13:796882
Bastide L et al (2022) Atypical acute disseminated encephalomyelitis with systemic inflammation after a first dose of AztraZaneca COVID-19 vaccine. a case report. Front Neurol. https://doi.org/10.3389/fneur.2022.995875
Cao L, Ren L (2022) Acute disseminated encephalomyelitis after severe acute respiratory syndrome coronavirus 2 vaccination: a case report. Acta Neurol Belg 122(3):793–795. https://doi.org/10.1007/s13760-021-01608-2
Engler RJM et al (2015) a prospective study of the incidence of myocarditis/pericarditis and new onset cardiac symptoms following smallpox and influenza vaccination. PLoS ONE 10(3):e0118283. https://doi.org/10.1371/journal.pone.0118283
Falahi S, Kenarkoohi A (2021) Sex and gender differences in the outcome of patients with COVID-19. J Med Virol 93(1):151–152. https://doi.org/10.1002/jmv.26243
Garg A, Batra PK, Gupta P (2023) Post COVID-19 vaccination acute disseminated encephalomyelitis: a case report. Curr Med Imag Rev 19(1):91–95
Goyal M et al (2023) Myocarditis post-SARS-CoV-2 vaccination : a systematic review. QJM an Int J Med 116(1):7–25
Grabie N, Lichtman AH, Padera R (2019) T cell checkpoint regulators in the heart. Cardiovasc Res 115(5):869–877
Gustavsen S, Nordling MM, Weglewski A (2023) Acute disseminated encephalomyelitis following the COVID-19 vaccine Ad26.COV2.S, a case report. Bull Nat Res Centre 47(1):5. https://doi.org/10.1186/s42269-023-00981-7
Huynh W et al (2008) Post-vaccination encephalomyelitis: literature review and illustrative case. J Clin Neurosci 15(12):1315–1322
Kania K, Ambrosius W, Kupczyk ET, Kozubski W (2021) Acute disseminated encephalomyelitis in a patient vaccinated against SARS-CoV-2. Ann Clin Transl Neurol 8(10):2000–2003. https://doi.org/10.1002/acn3.51447
Kenangil O, Gulay BC, Ari CG, Demir MK (2021) Acute disseminated encephalomyelitis-like presentation after an inactivated coronavirus vaccine. Acta Neurol Belg 121(4):1089–1091
Lazaro LG et al (2022) Acute disseminated encephalomyelitis following vaccination against SARS-CoV-2: A Case Report. Brain Behav Immun Health 20:100439
Li M et al (2021) Myocarditis and pericarditis following covid-19 vaccination: inequalities in age and vaccine types. J. Pers. Med. 11(11):1106
Lohmann L et al (2022) Severe disease exacerbation after MRNA COVID-19 vaccination unmasks suspected multiple sclerosis as neuromyelitis optica spectrum disorder: a case report. BMC Neurol 22(1):1–4. https://doi.org/10.1186/s12883-022-02698-y
Maramattom BV, Lotlikar RS, Sukumaran S (2022) Central nervous system adverse events after ChAdOx1 vaccination. Neurol Sci 43(6):3503–3507
Miyamoto K et al (2022) A case of anti-MOG antibody-positive ADEM following COVID-19 MRNA vaccination. Neurol Sci 43(6):3513–3514. https://doi.org/10.1007/s10072-022-06019-6
Mousa H, Patel TH, Meadows I, Ozdemir B (2022) Acute Disseminated Encephalomyelitis (ADEM) After Consecutive Exposures to Mycoplasma and COVID Vaccine: A Case Report. Cureus. https://doi.org/10.7759/cureus.26258
Mumoli L et al (2022) ADEM Anti-MOG Antibody-Positive after SARS-CoV2 Vaccination. Neurol Sci 43(2):763–766. https://doi.org/10.1007/s10072-021-05761-7
Nabizadeh F, Noori M, Rahmani S, Hosseini H (2023) Acute disseminated encephalomyelitis (ADEM) following covid-19 vaccination: a systematic review. J Clin Neurosci 111:57–70
Nagaratnam SA et al (2022) Acute disseminated encephalomyelitis with bilateral optic neuritis following ChAdOx1 COVID-19 vaccination. BMC Neurol 22(1):54. https://doi.org/10.1186/s12883-022-02575-8
Naoko N et al (2003) Neurologic complications associated with influenza vaccination: two adult cases. Intern Med 42(2):191–194
Netravathi M et al (2022) COVID-19 vaccine associated demyelination & its association with MOG antibody. Multip Sclerosis Relat Disorders 60:103739
Nimkar SV et al (2022) Fatal acute disseminated encephalomyelitis post-COVID-19 vaccination: a rare case report. Cureus. https://doi.org/10.7759/cureus.31810
Permezel F, Borojevic B, Lau S, de Boer HH (2022) Acute disseminated encephalomyelitis (ADEM) following recent oxford/astrazeneca COVID-19 vaccination. Forensic Sci Med Pathol 18(1):74–79. https://doi.org/10.1007/s12024-021-00440-7
Platt MP, Agalliu D, Cutforth T (2017) Hello from the other side: how autoantibodies circumvent the blood-brain barrier in autoimmune encephalitis. Front Immunol. https://doi.org/10.3389/fimmu.2017.00442/full
Raknuzzaman M, Jannaty T, Hossain MB, Saha B, Dey SK, Shahidullah M (2021) Post Covid19 vaccination acute disseminated encephalomyelitis: a case report in Bangladesh. Int J Med Sci Clin Res Stud 1(03):31–36
Rinaldi V et al (2022) ADEM after ChAdOx1 NCoV-19 vaccine: a case report. Mult Scler J 28(7):1151–1154. https://doi.org/10.1177/13524585211040222
Sazgarnejad S, Kordipour, V (2022) Acute Disseminated Encephalomyelitis Following Inactivated COVID-19 Vaccine : A Case Report Case Presentation. 62 11: 1673.
Sejvar JJ (2005) Neurologic adverse events associated with smallpox vaccination in the United States, 2002–2004. JAMA 294(21):2744. https://doi.org/10.1001/jama.294.21.2744
Shimizu M et al (2021) An 88-Year-old woman with acute disseminated encephalomyelitis following messenger ribonucleic acid-based COVID-19 vaccination. NeurologicalSci 25:100381
Simone AM et al (2021) Acute disseminated encephalomyelitis associated with anti-myelin oligodendrocyte glycoprotein (MOG-IGG) antibody in a patient with recent vaccination against SARS-CoV-2. J Neurol Sci 429:118167
Spindler KR, Hsu T-H (2012) Viral disruption of the blood-brain barrier. Trends Microbiol 20(6):282–290
Truong DT et al (2022) Clinically suspected myocarditis temporally related to COVID-19 vaccination in adolescents and young adults: suspected myocarditis after COVID-19 vaccination. Circulation 145(5):345–356. https://doi.org/10.1161/CIRCULATIONAHA.121.056583
Vogrig A et al (2021) Acute disseminated encephalomyelitis after SARS-CoV-2 vaccination. Clin Neurol Neurosurg 208:106839
Williams SE et al (2011) Causality assessment of serious neurologic adverse events following 2009 H1N1 vaccination. Vaccine 29(46):8302–8308
Wu X et al (2015) Acute necrotizing encephalopathy: an underrecognized clinicoradiologic disorder. Mediators Inflamm 2015:792578
Yazdanpanah F et al (2022) Acute disseminated encephalomyelitis (ADEM) after SARS- CoV-2 vaccination: a case report. Radiol Case Reports 17(5):1789–1793

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