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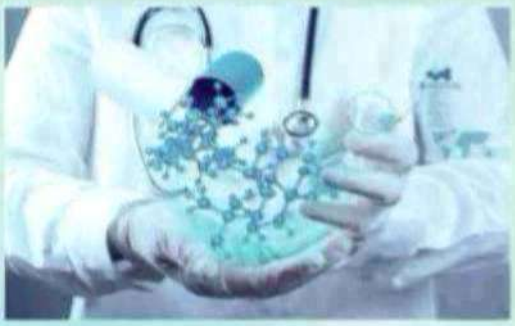

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NEW DAY IN MEDICINE

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ООО «ТИББИЁТДА ЯНГИ КУН»

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RISK FACTORS FOR THE DEVELOPMENT OF NEUROLOGICAL ADVERSE EVENTS AFTER COVID-19 VACCINATION

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✓ ***Resume***

The study analyzed the clinical and epidemiological characteristics of neurological adverse events following COVID-19 vaccination. It was shown that most neurological complications were mild and reversible. Individuals with a history of previous COVID-19 infection and those with vascular or metabolic comorbidities were more likely to develop post-vaccination neurological manifestations. The findings highlight the importance of careful post-vaccination observation and individualized risk assessment in patients with chronic diseases while confirming the overall safety and effectiveness of COVID-19 vaccines.

Keywords: COVID-19, vaccination, neurological complications, risk factors, arterial hypertension, diabetes mellitus, vaccine safety.

ФАКТОРЫ РИСКА РАЗВИТИЯ НЕВРОЛОГИЧЕСКИХ ОСЛОЖНЕНИЙ ПОСЛЕ ВАКЦИНАЦИИ ОТ COVID-19

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✓ ***Резюме***

Проведено исследование, посвящённое клиническим особенностям и факторам риска развития неврологических осложнений после вакцинации против COVID-19. Установлено, что большинство неврологических реакций имеют лёгкое и обратимое течение. Повышенная вероятность осложнений наблюдается у лиц с перенесённой коронавирусной инфекцией и хроническими сосудисто-метаболическими заболеваниями. Полученные данные подтверждают безопасность вакцин и подчёркивают необходимость индивидуального наблюдения пациентов с сопутствующей патологией.

Ключевые слова: COVID-19, вакцинация, неврологические осложнения, факторы риска, артериальная гипертензия, сахарный диабет, безопасность вакцин

COVID-19 VAKSINATSIYASIDAN KEYINGI NEVROLOGIK ASORATLAR RIVOJLANISHINING XAVF OMILLARI

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✓ ***Rezyume***

Tadqiqot COVID-19 ga qarshi emlashdan so‘ng kuzatilgan nevrologik asoratlarning klinik xususiyatlari va xavf omillariga bag‘ishlandi. Aniqlanishicha, aksariyat nevrologik reaksiyalar yengil kechadi va qaytuvchan bo‘ladi. COVID-19 infeksiyasini o‘tkazgan, shuningdek yurak-qon tomir yoki metabolik kasalliklarga ega shaxslar orasida asoratlar rivojlanish ehtimoli yuqoriroqdir. Olingan natijalar vaksinalarning xavfsizligini tasdiqlaydi hamda surunkali kasallikka ega bemorlarni individual kuzatish zarurligini ta’kidlaydi.

Kalit so‘zlar: COVID-19, emlash, nevrologik asoratlar, xavf omillari, arterial gipertenziya, qandli diabet, vaksina xavfsizligi

Relevance

The development of neurological adverse events following COVID-19 vaccination (NAE-COVID-19) appears to be multifactorially determined. Beyond vaccine platform or demographic features, pre-existing somatic diseases and a history of previous SARS-CoV-2 infection have emerged as major risk determinants influencing both the likelihood and severity of neurological complications. Evidence from cohort studies, meta-analyses, and our own retrospective investigation highlights the synergistic role of vascular, metabolic, and immune-inflammatory disorders in shaping susceptibility profiles [1–5].

History of Prior COVID-19 Infection. Previous SARS-CoV-2 infection is among the most relevant background factors in patients who subsequently develop neurological syndromes after vaccination. Persistent immune dysregulation, microvascular inflammation, and residual endothelial injury following even mild or moderate COVID-19 can predispose to exaggerated post-vaccination responses [5, 6]. Several studies demonstrated that post-COVID individuals exhibit elevated baseline IL-6, D-dimer, and Syndecan-1, markers reflecting chronic endotheliopathy and ongoing low-grade neuroinflammation [7, 8]. These findings align with those of Möller et al. (2023) and Rose-John et al. (2023), who reported persistent IL-6-driven inflammation and glycocalyx degradation months after viral recovery [9, 10].

Arterial Hypertension and Cerebrovascular Atherosclerosis. Chronic hypertension is one of the most consistent risk factors for post-vaccination cerebrovascular and neuropathic events [11, 12]. Long-standing pressure overload induces endothelial dysfunction, oxidative stress, and arterial remodeling, which collectively reduce cerebral vascular reserve. These mechanisms can potentiate immune-mediated microthrombotic or ischemic reactions after vaccination [13]. Neuroimaging revealed a higher prevalence of chronic small-vessel ischemic changes (Fazekas 1–2) and carotid atherosclerosis (≥30 % stenosis) among hypertensive patients with post-vaccination neurological syndromes. These results correspond with the observations of Chemaitelly et al. (2024) and Papadopoulos et al. (2022), who noted that vascular comorbidities significantly increase the likelihood of post-vaccination ischemic events, albeit at a rate still far below that seen during acute COVID-19 infection [14, 15].

Type 2 Diabetes Mellitus and Metabolic Syndrome. Metabolic dysregulation is another key determinant of endothelial vulnerability and altered immune response to vaccination. Type 2 diabetes mellitus (T2DM) promotes chronic inflammation, glycation-induced vascular injury, and reduced nitric-oxide bioavailability, thereby exacerbating post-vaccination microvascular reactivity [16–18]. Elevated fasting glucose correlated positively with IL-6 concentrations, indicating shared inflammatory pathways. Internationally, Faksova et al. (2024) and Klein et al. (2022) also reported that metabolic syndrome increases the odds of vaccine-related neurovascular symptoms, likely through endothelial glycocalyx degradation and altered cytokine signaling [19, 20].

Coronary Heart Disease and Cardiac Pathology. Patients with ischemic heart disease (IHD), atrial fibrillation, or chronic heart failure exhibit systemic endothelial injury and platelet hyperreactivity, which may potentiate immune-thrombotic phenomena following vaccination [21, 22]. Cardiac comorbidities were particularly common in those presenting with ischemic stroke or transient ischemic attacks post-vaccination, supporting the interplay between systemic vascular burden and neurovascular outcomes.

A global meta-analysis by Rafati et al. (2023) confirmed that pre-existing cardiovascular disease increases the likelihood of reported neurological AEFIs by 1.8-fold, primarily through overlapping microthrombotic mechanisms [23].

Atherosclerosis and Endothelial Dysfunction. Generalized atherosclerosis represents a final common pathway integrating many of the above factors. The disruption of endothelial homeostasis in atherosclerotic vessels leads to heightened cytokine responsiveness, impaired glycocalyx regeneration, and reduced tolerance to immune stressors [24, 25]. Liang et al. (2023) and Xu et al. (2024) similarly demonstrated that

high SDC-1 predicts poorer neurological outcomes due to endothelial glycocalyx loss and microvascular leak [26, 27].

These results confirm that neurological adverse events are multifactorially driven, arising at the intersection of pre-existing vascular disease, metabolic imbalance, and post-COVID endothelial inflammation, rather than from direct neurotoxicity of vaccine components.

Aim of the study: The present study aimed to comprehensively evaluate the risk factors and clinical characteristics of neurological adverse events following COVID-19 vaccination in a retrospective cohort of adult patients.

Materials and methods

This retrospective, comparative study was conducted between January 2022 and March 2024 at the Neurology Department of the multidisciplinary clinic of the Tashkent State Medical University, city clinical hospital №7 and the family hospital (Tashkent, Uzbekistan).

The study population comprised 90 adult patients aged 21 to 64 years, divided into two equal groups: main group (n = 45) — individuals who developed neurological complications within 30 days after receiving a COVID-19 vaccine; control group (n = 45) — vaccinated individuals without neurological manifestations, matched by age and sex. The mean age of all participants was 43.7 ± 11.5 years. The percentage of men and women 54,3% and 45,7%. There were no statistically significant differences in age or sex distribution between the two groups, ensuring their comparability.

All individuals underwent detailed neurological assessment performed by certified neurologists, including examination of cranial nerve function, motor and sensory systems, coordination, and reflexes. Neuroimaging methods such as magnetic resonance imaging (MRI) and computed tomography (CT) were used when indicated to confirm or exclude central nervous system lesions. In selected cases, electroencephalography (EEG), electromyography (EMG), and Doppler ultrasonography of cerebral vessels were performed.

Result and discussions

Among the 45 patients with neurological AEFIs, the spectrum of disorders was heterogeneous and included both central and peripheral nervous system involvement.
The most frequently observed complications were: ischemic stroke, Gullian-Barre syndrome, Bell's palsy, encephalitis, peripheral neuropathy, sensorineural hearing loss and others (dizziness, autonomic dysfunction). Most patients (74.5 %) developed symptoms after the first or second dose, typically within 5–14 days post-vaccination.

Comorbid diseases were more prevalent among patients with neurological AEFIs compared to controls: arterial hypertension (38%), type 2 diabetes mellitus (22%), coronary heart disease/arrhythmia (18%), generalized atherosclerosis (14%), history of COVID-19 infection (42%) ($p < 0.05$). Multimorbidity (≥ 2 comorbidities) was found in 32 % of patients in the main group compared with 10 % in controls ($p < 0.05$). Patients with multiple comorbidities demonstrated higher rates of ischemic and polyneuropathic manifestations.

Most patients experienced favorable outcomes with gradual resolution of symptoms. Complete recovery or marked improvement was achieved in 86 % of cases within 3 months, while 7 patients (14 %) had residual mild neurological deficits (mainly post-stroke or GBS). No deaths were recorded.

Conclusion

This study demonstrates that neurological adverse events following COVID-19 vaccination are rare, predominantly mild, and generally reversible, yet their occurrence is influenced by identifiable clinical and epidemiological factors.

The analysis revealed that patients with a history of prior COVID-19 infection, as well as those suffering from arterial hypertension, type 2 diabetes mellitus, coronary heart disease, or atherosclerosis, were significantly more likely to develop post-vaccination neurological manifestations compared with healthy vaccine recipients. Multivariate modeling identified previous COVID-19 infection and vascular-metabolic comorbidities as independent predictors of neurological adverse events, suggesting a role of persistent endothelial and immune dysfunction in their pathogenesis.

Despite these associations, the absolute risk remains extremely low, and the benefits of vaccination in preventing severe COVID-19 and its neurological sequelae far outweigh the risks. The findings underscore the importance of individual risk assessment and targeted post-vaccination monitoring in patients with vascular and metabolic comorbidities to ensure early detection and timely management of possible neurological complications.

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