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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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EVALUATION OF TNF-ALPHA LEVELS IN MALE PATIENTS WITH STROKE: PROGNOSTIC IMPLICATIONS

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Abstract.

Background/Objective: Following a stroke, activation of the immune system leads to a cascade of events collectively known as neuroinflammation, which involves the release of pro-inflammatory cytokines [such as tumor necrosis factor-alpha (TNF-α)], recruitment of immune cells, and disruption of the blood-brain barrier. Herein, we sought to investigate levels of TNF-α in patients with strokes (both ischemic and hemorrhagic).

Methods: Blood or serum specimens were collected from male patients with stroke from the Republic of Georgia (Adjarian) population. A total of 48 patients (ischemic stroke = 27; and hemorrhagic stroke = 21) formed the basis of this study analysis. An enzyme-linked immunosorbent assay (ELISA) was employed to assess the TNF-α levels in all specimens. The reference level was < 8 pg/mL. Statistical analyses were performed using GraphPad Prism 9. A p-value of <0.05 was considered statistically significant.

Results: Both ischemic and hemorrhagic stroke patients had relatively higher levels of TNF-α (15.26 ± 8.68 vs. 9.18 ± 5.66 pg/mL; p=0.0065). Approximately 1.66-fold increase in TNF-α level was observed in patients with ischemic stroke as compared to the hemorrhagic stroke patients.

Conclusion: Our analysis suggests that significantly increased levels of TNF-α are associated with both ischemic and hemorrhagic strokes male patients; however, the levels in ischemic stroke patients are more pronounced. Thus, monitoring/ targeting TNF-α may help identify high-risk patients and guide new therapeutic strategies to improve recovery in male stroke patients.

Key words. Ischemic stroke, hemorrhagic stroke, TNF-α, pro-inflammatory cytokines, cognitive impairments, prognostic factors.

Introduction.

Stroke is a widespread and severe global health problem, ranking among the top causes of death and disability worldwide. Its burden is increasing in absolute numbers, affecting millions of people across all regions and age groups [1]. Stroke is broadly classified into two main types: i) ischemic stroke, caused by an obstruction of blood flow to the brain, and ii) hemorrhagic stroke, resulting from bleeding into or around brain tissues [2]. While ischemic stroke accounts for approximately 80–85% of all cases, hemorrhagic stroke comprises about 15–20%. Although both types share common risk factors such as hypertension and diabetes, their pathophysiology and clinical outcomes differ significantly [3]. In men, who tend to experience strokes at a relatively younger age and with greater severity than women, understanding the underlying biological mechanisms is particularly important for improving prevention and treatment strategies [4].

Globally, stroke represents a significant burden on healthcare systems, with an increasing number of cases observed in low- and middle-income countries [1]. Men have a slightly higher lifetime risk of stroke compared to women and are also more likely to experience recurrent strokes. This gender difference may partially be explained by variations in lifestyle interventions, hormone levels, and immune responses [5]. Among the many biological processes involved in stroke development and progression, inflammation play a central role. Following a stroke, the activation of the immune system leads to a cascade of events collectively known as neuroinflammation. This process involves the release of pro-inflammatory cytokines, recruitment of immune cells, and disruption of the blood-brain barrier (BBB), all of which contribute to further brain injury [6].

One of the most studied cytokines in this context is tumor necrosis factor-alpha (TNF-α), which is a key pro-inflammatory molecule rapidly produced by immune and brain cells in response to injury. It contributes to neuronal damage by promoting oxidative stress, endothelial dysfunction, and increased permeability of the BBB [7]. Elevated levels of TNF-α have been observed in both ischemic and hemorrhagic stroke patients, and its expression is linked with worse clinical outcomes, including larger infarct size and poorer neurological recovery [8]. Despite its recognized role in stroke pathobiology, the specific patterns and implications of TNF-α expression in male stroke patients remain underexplored. Monitoring and targeting TNF-α may help identify high-risk patients and guide new therapeutic strategies to improve recovery in male stroke patients.

Sex hormones such as testosterone and estrogen are known to influence immune responses, and emerging evidence suggests that men may exhibit distinct inflammatory profiles following stroke. Understanding these differences may help explain variations in disease progression and recovery between the genders and could support the development of more targeted interventions [5]. Herein, we aimed to evaluate TNF-α levels in patients with strokes (both ischemic and hemorrhagic).

Materials and Methods.

This study included male patients with ischemic (n=27) and hemorrhagic (n=21) strokes from the Republic of Georgia (Adjarian) population. This study was approved by our primaly

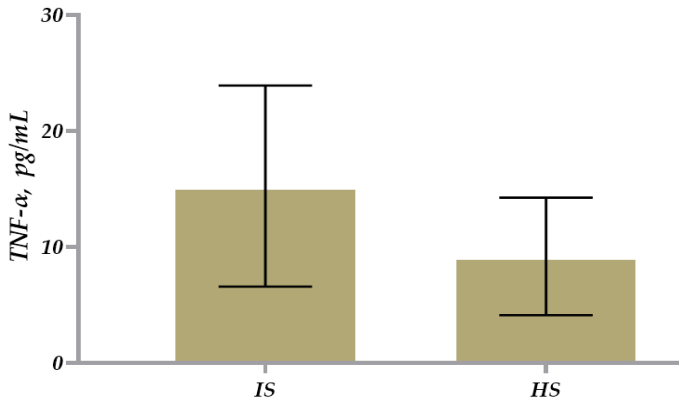
institutional review board / ethics committee.

For TNF-α analysis, venous blood specimens (plasma or serum) were used. An enzyme-linked immunosorbent assay (ELISA, R&D Systems, Minneapolis, USA) was employed to assess TNF-α levels. The reference level was < 8 pg/mL. Statistical analysis (t-test, descriptive statistics) of the experimental data was performed using GraphPad Prism 9; The p-level of < 0.05 was considered statistically significant.

Results.

The mean age of ischemic stroke patients was 73.30 ± 11.59 years and the hemorrhagic stroke patients was 59.90 ± 18.56 years. As shown in Figure 1, TNF-α levels were determined to be 15.26 ± 8.68 pg/mL in ischemic stroke specimens and 9.18 ± 5.66 pg/mL in hemorrhagic stroke specimens (p=0.0065). Approximately 1.66-fold increase was observed in the case of ischemic stroke as compared to the hemorrhagic stroke cases (Figure 1).

Figure 1. *The levels of tumor necrosis factor-alpha (TNF-α) in male patients with ischemic stroke (IS, n=27) and hemorrhagic stroke (HS, n=21) from the Republic of Georgia (Adjarian) population.*



It is widely recognized that in ischemic stroke, the brain does not get enough blood and oxygen, which leads to inflammation. One of the main inflammatory proteins involved is TNF-α. It is produced quickly by brain cells like microglia and by immune cells. TNF-α increases damage by making the BBB leaky, reducing blood flow, and increasing cell death [9].

Studies show that TNF-α levels go up in men after ischemic stroke. For example, high TNF-α was found in both cerebrospinal fluid and blood of stroke patients during the first 24 hours [10]. High TNF-α levels are often linked with larger strokes, higher NIH Stroke Scale scores, and worse outcomes [11]. Some men may also have genetic changes that affect TNF-α production. The -308 G/A polymorphism in the TNF gene is one such variant. People with the A allele may produce more TNF-α and have a higher stroke risk [12].

Discussion.

In animal models, blocking TNF-α has been shown to reduce brain damage and improve outcomes. However, these treatments have not yet been proven in humans. More research is needed, especially in male stroke patients [13].

In a hemorrhagic stroke, bleeding occurs in the brain. This causes early injury, swelling, and damage to nearby brain tissue. TNF-α plays a key role in this process. It is released soon after the bleed and causes BBB disruption, inflammation, and may lead to hematoma expansion [9].

Human studies have demonstrated that TNF-α levels increase following intracerebral hemorrhage. For example, studies have found that higher serum TNF-α levels are associated with larger hematoma sizes and worse outcomes [14]. Compared to ischemic stroke, TNF-α levels may rise earlier in hemorrhagic stroke due to the sudden presence of blood in brain tissue. TNF-α is also linked with perihematomal edema, which increases pressure and damage [9].

In the long-term, high TNF-α levels can lead to chronic inflammation and impede recovery. In men, this may be exacerbated by stronger inflammatory responses [15]. More studies are needed to understand how TNF-α affects male patients after hemorrhagic stroke and whether it can be used as a target for treatment. In ischemic stroke, TNF-α levels rise gradually as brain cells die and inflammation develops. In hemorrhagic stroke, TNF-α increases more rapidly due to the presence of blood in the brain, leading to immediate immune activation [16]. These differences may be due to oxidative stress and the varying responses of microglia (brain immune cells) in each type. Ischemia leads to slow oxygen loss and cell damage, while hemorrhage causes direct tissue irritation and swelling. This leads to different patterns of TNF-α release [17].

Sex hormones also affect inflammation. Androgens (male hormones) may increase TNF-α production, while estrogens (female hormones) can reduce it. This may explain why men show higher TNF-α responses and more severe inflammation after stroke [18]. Understanding these differences can help in designing gender-specific treatments for stroke [19].

Anti-TNF drugs, used in other diseases like rheumatoid arthritis, show promise in stroke models. These drugs can reduce inflammation and brain damage. However, using them in stroke has challenges. Timing is critical; blocking TNF-α too early or too late may harm rather than help [20]. More safety data is also needed in humans. Personalized medicine is essential after a stroke. Since men may have stronger TNF-α responses, they might benefit more from TNF-targeted treatments. Current stroke trials rarely focus on gender-specific differences [21]. Hence, more clinical trials are needed, especially those that include male-only or gender-stratified analyses, to better understand treatment effects.

Current research on TNF-α in stroke has several limitations. Many studies have small sample sizes and include mixed populations, making it hard to understand sex-specific effects. There is also a lack of male-only studies, resulting in limited data on men [22]. Another issue is the variation in how TNF-α is measured; different methods, sample types, and time points reduce consistency across studies. Future research should use standardized protocols for measuring TNF-α over time [23]. There is also a need for long-term studies to see how TNF-α levels change after stroke and how they relate to recovery in men. Combining proteomic (protein-level) and genetic data could potentially help identify which patients are most affected by TNF-α and who may benefit from targeted treatment [24].

More focused research will help improve stroke care for men and guide personalized therapy based on TNF-α levels.

Elevations have shown an association with worse neurological outcomes, which may contribute to neuronal death [25]. According to this study, higher TNF-α levels are significantly associated with increased risk of post-stroke cognitive impairment, suggesting its value as a prognostic biomarker [25]. Notably, serum TNF levels increase early and are prolonged after stroke onset, regardless of lesion size, neurological impairment, age, gender, vascular risk factors, or infectious complications [26]. Based on the meta-analysis of individual participant data from randomized controlled trials (including men and women with acute ischemic stroke), women with ischemic stroke had better survival outcomes but also with more disability and poorer quality-of-life, with variations in hospital and out-of-hospital control potentially contributing to these disparities [27].

Thus, TNF-α plays a critical role in both strokes, accordingly associated with worse outcomes; moreover, it increases brain damage, particularly in male patients [28]. The differences in TNF-α dynamics necessitate further research focused on gender-specific responses. Understanding the role of TNF-α can lead to personalized treatment strategies that enhance recovery and improve outcomes for stroke patients.

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Conflict of interest.

The authors declare no conflict of interest.

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