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EDITORIAL

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Volume 2

It is with great pride and enthusiasm that we present the second volume of Essentials of Frontline Medicine Journal (ISSN: 3062-1704). This milestone marks more than just the continuation of our publication—it signifies our growing presence and recognition in the academic community. We are especially pleased to announce that our journal is now indexed by Google Scholar, a significant step forward in increasing the visibility and accessibility of the valuable research we publish.

Being searchable through Google Scholar ensures that the work of our contributors can reach a broader audience, fostering greater academic engagement and encouraging citations that help shape the future of medical knowledge. It also affirms the quality and relevance of our journal in a competitive and rapidly evolving landscape of scientific publishing.

We extend our sincere gratitude to our editorial board, reviewers, and authors—whose dedication and academic integrity have made this achievement possible. Your continued support and contributions are vital as we strive to build a platform that promotes rigorous research, clinical insight, and interdisciplinary dialogue.

As we turn the page to this new chapter, we reaffirm our commitment to excellence in medical publishing and invite you to explore, share, and contribute to future volumes of Essentials of Frontline Medicine Journal (ISSN: 3062-1704).

Sincerely,

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Original Article

Readability Analysis of Turkish Internet Content on Varicose Veins

Murat EROĞLU^{1*}

¹ Department of Cardiovascular Surgery, Kütahya Health Sciences University, Kütahya, Türkiye

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 *Corresponding author: Murat EROĞLU, Department of Cardiovascular Surgery, Kütahya Health Sciences University, Kütahya, Türkiye. E-mail: murateroglu5961@hotmail.com

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ABSTRACT

Objective: Internet is one of the most widely used sources for health information. However, the comprehensibility of this content is critical for individuals' health literacy. This study examines the readability level of Turkish health content on "varicose veins" on the internet.

Methods: In the study, the contents of 30 websites ranked in the top 10 in Google, Yandex and Bing search engines for the word "varicose veins" were evaluated and 19 websites were analyzed after excluding the inappropriate ones. The texts were analyzed using two Turkish-specific readability formulas, Ateşman and Bezirci-Yılmaz formulas.

Results: According to Ateşman's formula, the average readability score of the texts was 54.0±6.1, indicating that these contents are comprehensible by individuals with 9th grade and above education level. Bezirci-Yılmaz scores averaged 10.6±2.1, indicating that some texts were simple while others were quite complex.

Conclusion: The vast majority of the health content on the analyzed websites requires a reading level above the recommended education grade level. This may negatively affect the access to and understanding of information, especially by individuals with low education levels. Therefore, presenting health content in a simpler and more understandable language would be an important step in increasing the overall health literacy of the population.

Keywords: Health literacy, internet, search engines, varicose vein

INTRODUCTION

Internet has been increasingly used in our country in recent years. The Turkish Statistical Institute reported internet usage in Turkey as 88.8% (1). Increasingly, internet users access information through websites by using search engines (2).

Changing demographics, advances in treatments and increasing health needs require more up-to-date and accessible health information, and with easier access to the internet, individuals' habits of seeking and using health information have changed, with many people turning to online resources before seeking a professional diagnosis. These searches are often related to personal health concerns, diseases and treatment options. Moreover, people are seeking this information not only for themselves but also for others. The increased search for health information online may change the way patients interact with their doctors and evaluate their health decisions (3). When looking at how most individuals access health-related information online, the most common method is through searches using search engines. By providing a fast, easily accessible and lowcost opportunity to obtain personalized information about health conditions and preventive measures, search engines help users make informed health decisions (4).

While patients used to obtain health information from health personnel more frequently in the past, they try to obtain information from different sources due to intensive work of health professionals (5). For this purpose, many written sources are used to obtain information. The extent to which written sources can be understood by the reader can be measured by readability (6,7). For this purpose, various formulas have been developed to measure the readability of Turkish written texts (5-8).

The readability and comprehensibility of health-related materials has been shown to directly influence patient knowledge (9). Although many resources are available online, there are publications showing that these resources are not readable and accessible. Previous evidence has shown that medical information for patients is written at a higher reading level than that of the average adult (10).

In this study, the content on the subject of "varicose veins" on the internet was evaluated using two different Turkish-specific readability formulas- Ateşman and Bezirci-Yılmaz.

METHODS

This cross-sectional study was conducted using the most frequently used search engines in Turkey (11), Google, Yandex, Bing. On 15.03.2025, the keyword "varicose veins" was searched and the first 10 websites in each search engine were evaluated. All history and cookie information of the internet browser (Google Chrome) was deleted in order to prevent the search results from being affected by previous browser history and cookies. At the beginning of the study, it was planned to exclude websites that opened in other languages during the search, websites with sponsored links and advertisements, forum sites where detailed information can only be viewed with paid membership, websites that are not related to the search term, and websites that only contain videos such as YouTube.

The texts obtained from each site were analyzed according to their structural features such as the number of sentences, words, letters, characters, syllables and polysyllabic words, and the texts obtained as a result of the study were evaluated with Ateşman and Bezirci-Yılmaz readability formulas (12-13). For this purpose, the software developed by Bezirci-Yılmaz was used (13). With the software, the number of sentences, number of words, number of letters, number of characters, number of syllables, number of words with more than 4 syllables, Ateşman readability score, Bezirci-Yılmaz scores were obtained.

Ateşman's readability formula was developed in 1997 to measure Turkish readability. An increase in the score indicates an increase in readability (12) and is calculated as:

Readability score = 198.825- 40.175 x word length (total syllables total words)- 2.610 x sentence length (total words/total sentences).

Bezirci-Yılmaz readability formula was developed in 2010 to measure Turkish readability and is calculated as:

Readability score= √OKS x [(H3 x 0.84) + (H4 x 1.5) + (H5x3.5) + (H6 x 26.25)]

OKS: average word count; H3: mean number of 3-syllable words; H4: mean number of 4-syllable words; H5: mean number of 5syllable words; H6: the average number of words with 6 or more syllables. Readability decreases as the score obtained from the scale increases (13).

All collected data were evaluated with SPSS, Version 23.0 (IBM Corp., Armonk, NY, USA). Mean \pm standard deviation and median (minimum-maximum) were used for descriptive data. Results were expressed as numbers and percentages for categorical data.

The study was conducted in accordance with ethical research principles. The websites examined in our study are publicly accessible platforms, therefore our study did not require specific ethical committee approval and did not require informed consent from participants.

RESULTS

Since Internet users usually look at the first 10 results when using a search engine (2), the first 10 sites in Google, Yandex, Yahoo search engines were evaluated in our study.

When the keyword varicose veins was searched with the Google search engine, it was seen that eight websites belonged to the corporate sites of private hospitals and one belonged to the personal site of a healthcare worker. One search result belonged to the YouTube channel of a private hospital and was excluded from the evaluation for readability

A search with the Yandex search engine revealed that nine results belonged to private hospitals and one to a public hospital.

In the search conducted with the Bing search engine, it was determined that seven results belonged to private hospitals, one to a blog site, one to a health website that publishes various healthrelated publications and one to a magazine.

As a result of a total of 30 searches, three websites appeared in all three search engines. As shown in Tables 1, 2 and 3, the sites are indicated by numbers.

Site no	Type of website	Number of Sentences	Number of Words	Number of Letters	Number of characters	Number of Syllables	Number of Words with More Than 4 Syllables
1	Private hospital	38	380	2565	3011	1079	102
2	Private hospital	280	3566	24020	28226	10268	1082
3	Private hospital	151	1671	11514	13543	4914	530
4	Private hospital	115	1023	7243	8484	3077	337
5	Youtube channel	-	-	-	-	-	-
6	Private hospital	51	531	3655	4284	1564	168
7	Private hospital	100	1006	7110	8287	3020	342
8	Private hospital	84	688	4704	5558	1995	209
9	Private hospital	34	462	3246	3802	1365	150
10	Kişisel web sitesi	34	476	3400	3943	1446	167

Table 1. Search results with the keyword "varicose veins" in the Google search engine.

Table 2. Search results for the keyword "varicose veins" in the Yandex search engine.

Site no*	Type of Website	Number of Sentences	Number of Words	Number of Letters	Number of Characters	Number of Syllables	Number of Words with More Than 4 Syllables.
11	Private hospital	187	2451	16704	19594	7112	744
12	Private hospital	134	1083	7402	8723	3169	333
13	Private hospital	106	1270	8651	10179	3680	410
14	Private hospital	62	662	4363	5199	1841	173
15	Public hospital	74	649	4399	5214	1865	182

*Websites 1, 2, 4, 7, 8 also appeared in the top 10 results of the Yandex search

Table 3. Bing search engine search results for the keyword "varicose veins"

Site no*	Type of Website	Number of Sentences	Number of Words	Number of Letters	Number of Characters	Number of Syllables	Number of Words with More Than 4 Syllables
16	Blog site	85	974	6698	7919	2854	308
17	Private hospital	80	800	5208	6196	2234	218
18	Private hospital	126	1470	10052	11814	4278	471
19	Health blog	101	1117	7454	8736	3183	324
20	Magazine journal	156	1305	8771	10387	3709	364

*Websites 1, 2, 4, 11, 12 also appeared in the top 10 results of the Bing search

The average number of sentences in the evaluated texts was found to be 105.2 ± 60.2 , the average number of words was 1136.0 ± 772.5 , whereas the average number of letters was 7745.2 ± 5214.8 , also the average number of characters was 9110.5 ± 6122.8 , however the average number of syllables was 3297.5 ± 2229.5 , and the average number of polysyllabic words (with more than four syllables) was 348.1 ± 236.85 . The mean Ateşman readability score of the texts was 54.0 ± 6.1 , and the mean Bezirci-Yılmaz readability score was 10.6 ± 2.1 . According to Ateşman's fomula, readability levels were found to be 9th or 10th grade education and above. According to the Bezirci-Yılmaz score, 3 sites required primary school education and above, and 4 sites required university education and above (Table 4).

Table 4. Website's readability score and education level of the score.

Site no	Atoomon Coord	Education level towards Ateşman	Bezirci-Yılmaz	Education level towards Bezirci-
Site no	Ateşman Score	Can be read by anyone with a:	Score	Yılmaz
1	58.65	11th or 12th grade education	8.81	High school
2	49.9	13th or 15th grade education	12.3	University
3	51.8	11th or 12th grade education	10.88	High school
4	54.77	11th or 12th grade education	8.73	High school
5	-	-	-	-
6	53.32	11th or 12th grade education	10.5	High school
7	51.96	11th or 12th grade education	10.38	High school
8	60.95	9th or 10th grade education	7.98	Primary school
9	44.66	13th or 15th grade education	14.65	University
10	40.24	13th or 15th grade education	14.78	University
11	48.04	13th or 15th grade education	12.63	University
12	60.17	9th or 10th grade education	7.98	Primary school
13	51.14	11th or 12th grade education	11.59	High school
14	59.23	11th or 12th grade education	10.05	High school
15	60.49	9th or 10th grade education	8.65	High school
16	51.2	11th or 12th grade education	11.16	High school
17	60.54	9th or 10th grade education	9.15	High school
18	51.46	11th or 12th grade education	11.95	High school
19	55.48	11th or 12th grade education	10.98	High school
20	62.81	9th or 10th grade education	7.89	Primary school

DISCUSSION

Internet has become an important resource that individuals frequently use to access health information. Especially in searches related to chronic and common diseases, users generally use search engines first and obtain information based on the content they Access (3-4). However, the extent to which this information is comprehensible depends on the readability of the texts as well as the health literacy level of individuals (14).

In our study, we evaluated the health content obtained from 19 different websites accessible on the internet using the keyword "varicose veins" according to Ateşman and Bezirci-Yılmaz readability formulas. The majority of the sites evaluated were private hospital websites, but there were also some personal health blogs and websites managed by physicians.

The readability scores of the texts analyzed are distributed in a wide range. According to Ateşman's formula, the scores vary between 40 and 60, and these values indicate that the texts can generally be understood by individuals with intermediate reading skills. In other words, the readability of the texts of the analyzed websites is at least above the 9th or 10th grade education level. However, it is noted that the recommended readability level for health-related information is usually 8th grade or below (9, 14).

Texts written in the field of health are expected to be appropriate to the knowledge level of the target audience, contain simplified and structurally understandable texts in which medical terms are explained. In particular, the readability of the content on the websites of health service providers directly affects the capacity of individuals to make informed decisions (15).

According to the Bezirci-Yılmaz formula, the scores ranged between 8 and 15, indicating that some of the content was written relatively simply, but some of it was more academic and complex. In a study conducted by Demirci et al. in Turkey, it was observed that there was a significant increase in the frequency of searching for health information on the internet as the level of education increased, and that health literacy problems may occur in people with low levels of education (3). Again, statistical data show that internet use increases as the level of education increases (1,3). Despite all these data, this relationship between the level of education and the behavior of searching for health information on the internet can be explained by the fact that those with low levels of education give up the behavior of searching for information online because they cannot understand the information as a result of the complexity of the information they Access.

In our study, the most common readability level was determined as "barely readable". This result coincides with the findings of previous readability studies conducted in Turkey for various disease groups. For example, in a study conducted by Saldırım et al. on the readability of internet content on tinnitus, it was reported that the majority of the content was suitable for individuals at high school level and above, while it was difficult to understand for the general public (16). Similarly, Eyüboğlu found that the readability of internet on measles was low and insufficient in terms of health literacy (17).

Similar trends exist internationally. In a study by Berland et al., it was emphasized that the quality and readability of health information on the internet is variable and that the content is often loaded with medical terms and complex in structure (18). In the systematic review by McInnes and Haglund, it was found that the readability levels of patient information texts were mostly higher than the level recommended by the American health authorities (19).

The Ateşman, Bezirci-Yılmaz and Çetinkaya-Uzun readability formulas used in our study provide an objective measurement based on word and sentence lengths specific to Turkish language structure. These formulas have been previously applied in different medical fields and similar results were obtained. They stated that these formulas are limited especially in terms of depth of meaning when evaluating readability, but they are sufficient for a basic level evaluation (20).

The main limitation of these formulas is that they are based only on word and sentence lengths. It does not take into account other important components such as visual elements, headings, emphasis elements, clarity of language, and style of expression (21). In addition, since individual variables such as the level of health literacy, emotional state and motivation to access information may also affect readability, the results of this study should be interpreted in this context. Considering that the level of health literacy in Turkey is still low, such simplification efforts are likely to contribute positively to public health (22). Readability is an important factor in Internet users' access to health-related information, and the use of plain, understandable language helps users increase their knowledge about health conditions to self-manage their health conditions and improve their quality of life. Poor readability can lead to misinformation, inappropriate care and other potential harms (23). Some sites were found to use very simple and accessible language, while others offered more technical and academic content. This may make it difficult for individuals with low health literacy to understand the information. It is important for healthcare providers to provide simplified content while preparing texts, taking into account the knowledge level of the target audience.

Limitations

This study has some limitations. First, only content from 20 websites was analyzed. A broader search using different search engines and keyword combinations may provide more generalized results. In addition, the content was analyzed only in Turkish language and in text format.

Since the Internet is growing day by day, users' search results and site contents may change over time. In addition, the analysis is based only on written texts and the impact of visual or interactive content is not evaluated. At the same time, the typeface and font size used in the analyzed texts were not taken into account.

CONCLUSION

Nowadays, the public's need for effective, understandable consumer health resources is increasing due to the importance of individuals as active partners in health care. We found that the readability of Turkish websites providing information about varicose veins was higher than the average education level in Türkiye. It would be useful to develop easy-to-read websites for varicose vein patients to obtain information about their disease. In future studies, more extensive internet scans should be conducted and different types of content (video transcripts, social media posts, etc.) should be included. In addition, healthcare organizations should use digital tools that measure readability levels when preparing content and present articles in a simpler, publicly understandable language. Basic training in copywriting and health communication for health professionals can improve the quality of written information materials. Readability analysis should be used as a routine control tool in the content production process.

DECLARATIONS

Ethical Consideration: The websites examined in our study are publicly accessible platforms, therefore our study did not require specific ethical committee approval and did not require informed consent from participants. **Authorship Contributions:** This study is entirely one author's own work.

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Conflict of Interest Statement: There are no potential conflicts of interest to declare.

Data Availability Statement: The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

REFERENCES

- Türkiye İstatistik Kurumu. Hane Halkı Bilişim Teknolojileri Kullanım Araştırması 2024 [Internet]. 2024 [cited 2025 Mar 15]. Available from: https://data.tuik.gov.tr/Bulten/Index?p=Hanehalki-Bilisim-Teknolojileri-(BT)-Kullanim-Arastirmasi-2024-53492
- Atay C, Alanyalı M, Uyan SB, Baş C. Arama motoru optimizasyonu. Akademik Bilişim. 2010;10:10-12.
- Demirci Ş, Uğurluoğlu Ö, Konca M, Çakmak C. Socio-demographic characteristics affect health information seeking on the Internet in Turkey. Health Information & Libraries Journal. 2021;38(4):304-312.
- Bachl M, Link E, Mangold F, Stier S. Search engine use for healthrelated purposes: Behavioral data on online health informationseeking in Germany. Health Communication. 2024;39(8):1651-1664.
- Gürsoy E, Taştan K, Nas MA, Kartal İBY. Evaluation of summary of product characteristics and patient information leaflet of the bestselling drugs in Turkey in terms of readability. İstanbul Journal of Pharmacy. 2022;52(3):342-348.
- Ay IE, Duranoğlu Y. Göz damlası prospektüslerinin okunabilirlik düzeyinin değerlendirilmesi. Anatolian Clinic the Journal of Medical Sciences. 2022;27(1):55-59.
- Ay IE, Doğan M. An evaluation of the comprehensibility levels of ophthalmology surgical consent forms. Cureus. 2021;13(7):e17189.
- Er A, Ay IE, Ceran TH. Evaluating Turkish readability and quality of strabismus-related websites. Cureus. 2024;16(4):e17189.
- Temel MH, Erden Y, Bağcıer F. Information quality and readability: ChatGPT's responses to the most common questions about spinal cord injury. World Neurosurgery. 2024;181:e1138-e1144.
- Restrepo E, Ko N, Warner ET. An evaluation of readability and understandability of online education materials for breast cancer survivors. Journal of Cancer Survivorship. 2024;18(2):457-465.
- Novasta Bilişim Ltd. Şti. Türkiye'deki arama motoru kullanım oranları [Internet]. 2024 [cited 2025 Mar 15]. Available from: https://novasta.com.tr/turkiyede-ki-arama-motoru-kullanimoranlari/
- Ateşman E. Türkçede okunabilirliğin ölçülmesi. Dil Dergisi. 1997;58:71-74.
- Bezirci B, Yılmaz AE. Metinlerin okunabilirliğinin ölçülmesi üzerine bir yazılım kütüphanesi ve Türkçe için yeni bir okunabilirlik ölçütü. Dokuz

Eylül Üniversitesi Mühendislik Fakültesi Fen ve Mühendislik Dergisi. 2010;12(3):49-62.

- Gu JZ, Baird GL, Guevara AE, Sohn YJ, Lydston M, Doyle C, et al. A systematic review and meta-analysis of English language online patient education materials in breast cancer: Is readability the only story? The Breast. 2024;103:102322.
- Keselman A, Logan R, Smith CA, Leroy G, Zeng-Treitler Q. Developing informatics tools and strategies for consumer-centered health communication. Journal of the American Medical Informatics Association. 2008;15(4):473-483.
- Saldırım HB, Eren M, Kurtuluş N, Kırlaroğlu SN, Şerbetçioğlu MB. Tinnitus ile ilgili çevrim içi hasta bilgilendirme materyallerinin okunabilirliğinin değerlendirilmesi. Balkan Sağlık Bilimleri Dergisi. 2023;2(1):1-6.
- Eyüboğlu E. Ebeveynler ve online sağlık bilgisi arama davranışı: sağlık okuryazarlığı kapsamında bir inceleme. TRT Akademi. 2023;8(19):904-933.
- Berland GK, et al. Health information on the Internet: Accessibility, quality, and readability in English and Spanish. JAMA. 2001;285(20):2612-2621.
- McInnes N, Haglund BJ. Readability of online health information: Implications for health literacy. Informatics for Health and Social Care. 2011;36(4):173-189.
- Temur T. Okunabilirlik (Readability) Kavramı. Türklük Bilimi Araştırmaları. 2003;13:169-179.
- Orgun F, Paylan Akkoç C. Hasta eğitim materyallerinin değerlendirilmesi: Okunabilirlik formülleri ve materyal değerlendirme araçları. Turkiye Klinikleri Journal of Nursing Sciences. 2020;12(3):e1e8.
- T.C. Sağlık Bakanlığı. Türkiye Sağlık Okuryazarlığı Araştırması [Internet]. 2014 [cited 2025 Mar 15]. Available from: https://ekutuphane.saglik.gov.tr/Ekutuphane/kitaplar/SOYA%20R APOR.pdf
- Daraz L, Morrow AS, Ponce OJ, et al. Readability of online health information: A meta-narrative systematic review. American Journal of Medical Quality. 2018;33(5):487-492.

Cyberchondria and Health Anxiety Among Caregivers of Home Healthcare Patients in Eastern Türkiye

Merve ÖZÇINAR¹, Ersan GÜRSOY^{2*}

Original Article

¹ Family Medicine Specialist, Çatak Family Health Center, Van, Türkiye

² Department of Family Medicine, Erzincan Binali Yıldırım University, Medical Faculty, Erzincan, Türkiye

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*Corresponding author: Ersan GÜRSOY, Department of Family Medicine, Erzincan Binali Yıldırım University, Medical Faculty, Erzincan, Türkiye. E-mail: <u>ersangursoy@gmail.com</u> Cite This Article as: Özçınar M, Gürsoy E. Cyberchondria and Health Anxiety Among Caregivers of Home Healthcare Patients in Eastern Türkiye. Essentials Frontline Med J. 2025:2(1); 7-13.

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ABSTRACT

Objective: This study investigates the relationship between cyberchondria and health anxiety among caregivers of home healthcare patients in Eastern Türkiye.

Methods: In a cross-sectional design conducted from May to July 2023, 240 family members of home healthcare patients were assessed using the Cyberchondria Severity Scale (CSS-12) and the Health Anxiety Inventory (HAI). Socio-demographic data, caregiving duration, and online health information-seeking behaviors were also examined.

Results: The participants reported average scores of 22.36 (\pm 11.63) on the CSS-12 and 17.69 (\pm 11.54) on the HAI. On average, caregivers spent 0.48 hours per day on online health searches. A strong positive correlation (r = 0.404, p < 0.001) was found between cyberchondria and health anxiety scores. While cyberchondria and health anxiety levels were not significantly influenced by marital status, education, or relationship to the patient, a higher level of cyberchondria was observed among female participants (p < 0.001).

Conclusion: The study demonstrates a significant positive correlation between cyberchondria and health anxiety among caregivers, with a noticeable impact on female caregivers. These results highlight the need for psychological support for caregivers in home healthcare settings and further research into the effects of online health information-seeking behaviors on caregiver mental health.

Keywords: Cyberchondria, health anxiety, anxiety disorders, home care service, online health information, caregiver stress

INTRODUCTION

Home healthcare is a pivotal service that enables individuals to receive care within their living spaces, surrounded by family and friends (1). This model of care allows patients to distance themselves from the stressors of a hospital environment, potentially accelerating their recovery and enhancing their quality of life (2). However, caregivers of patients receiving home care might constantly experience concern and anxiety regarding the health status of their patients (3).

Recent studies indicate that caregivers engaging in excessive online searches for health-related information, a behavior known as cyberchondria, tend to experience heightened levels of health anxiety (4, 5). Cyberchondria, characterized by amplified anxiety due to excessive online health information seeking, is particularly prevalent among individuals who face uncertainty about health conditions, like caregivers of home healthcare patients (6, 7).

On the other hand, health anxiety is characterized by an individual's persistent belief that they have a serious illness, leading to associated distress (8). This condition can compromise an individual's daily quality of life and elevate psychological stress levels (9). Cyberchondria and health anxiety are closely linked, with cyberchondria often serving as a precursor to or exacerbating factor in health anxiety (10).

The evidence suggests that caregivers, in the absence of continuous professional health support that a hospital environment provides, may turn to online sources for information, potentially elevating levels of cyberchondria and inducing health anxiety (4). This exploration is crucial, as it can lead to better understanding and management of these psychological challenges faced by caregivers in the home healthcare setting.

The relationship between cyberchondria and health anxiety, especially concerning caregivers of home healthcare patients, presents a significant research avenue. To the best of our knowledge, no specific study in the literature addresses the relationship between levels of cyberchondria and health anxiety among relatives of patients receiving home healthcare. However, investigating these phenomena concurrently can augment the existing knowledge base and aid in developing strategies to preserve and support individuals' psychological health.

This study explores the relationship between cyberchondria levels and health anxiety among relatives of patients receiving home healthcare. By delving into the intricate relationship between these two phenomena, we aim to identify the factors influencing cyberchondria and health anxiety among caregivers. This will contribute to the literature and inform interventions to support the psychological well-being of home healthcare patients' relatives.

METHODS

Study Design

This research is characterised by a cross-sectional and descriptive design conducted between May and July 2023 at a tertiary hospital located in the eastern region of Türkiye.

Study Population and Sample

The study population comprises relatives of patients visited by the hospital's home healthcare unit during the specified dates. In the related home healthcare unit, services were provided to approximately 300 patients per month, amounting to around 600 patients over a two-month period. The sample size was calculated based on parameters N=600, d=0.05, p=0.5, and q=0.5, resulting in a size of 235. However, 240 individuals who met the inclusion criteria were incorporated into the study. This number represented approximately 20% of the total registered patient population, which amounted to around 1200 individuals. In sample selection, stratified random sampling method was used to ensure demographic diversity and representativeness of the general population structure of the region.

Inclusion criteria are as follows:

• Age range between 18-65 years

 Possessing the cognitive ability to respond to the questions in the study

· Being an internet user

• Being primarily responsible for the care of a patient receiving home healthcare

Exclusion criteria include:

· Being a healthcare worker or retired from healthcare

· Unwillingness to participate in the study

Data Collection Tools

A face-to-face interview technique was employed for data collection. The survey form consists of three sections: sociodemographic data, a Short Form of the Cyberchondria Severity Scale (CSS-12), and a Health Anxiety Inventory (Short Version). The researchers developed the first section, a 19-question survey form after a literature review, inquiring about participants' sociodemographic data, time spent online, and the care burden of the patient they are looking after. The second section utilised the 'Short Form of the Cyberchondria Severity Scale' to determine participants' levels of cyberchondria, and the third section employed the 'Health Anxiety Inventory (Short Version)' to gauge participants' levels of health anxiety. Since the CSS-12 and HAI used in our study are traditionally designed for self-assessment, these scales were completed by the participants.

The Short Form of the Cyberchondria Severity Scale (CSS-12) was initially developed by McElroy and Shevlin (2014) as a 33-item Likert-type scale (11). It was later condensed into a 12-item short form by the same authors in 2019. The Turkish validity and reliability of the short form were conducted by Söyler et al. in 2021(12). The CSS-12 is designed to assess the severity of individuals searching for disease symptoms online and comprises four sub-dimensions (Compulsiveness, Distress, Reassurance, and Compulsion). Items are scored using a five-point scale ranging from 1 (Never) to 5 (Always). The total score can range from 0 to 60, with higher scores indicating higher levels of cyberchondria. There are no reverse-scored items in the scale (13).

Health Anxiety Inventory (HAI) was developed by Salkovskis et al. in 2002 to measure individuals' health anxieties (14). The Turkish validity and reliability of the scale were conducted by Aydemir et al. in 2013(15). The inventory contains 18 items, each with four different options. Scoring for each item ranges from 0-3, with

higher scores indicating elevated levels of health anxiety. The maximum score attainable is 54, with scores above 27 indicating high anxiety (14).

Ethical Considerations

Ethical approval for this study was obtained from the local Clinical Research Ethics Committee on 30.03.2023, with the decision number 2023/07-5. Both verbal and written consent were acquired from participants before data collection, and all stages of the study adhered to the principles of the revised Helsinki Declaration.

Data Analysis

Data was analysed using IBM SPSS Statistics 23 (SPSS, Chicago, IL). The normality of data distribution was assessed using the Kolmogorov-Smirnov test. Descriptive statistics were presented as frequency and percentage for categorical data and mean and standard deviation or median and min-max values for numerical data. The Mann-Whitney U test was used for comparing two independent groups, the Kruskal-Wallis test for comparing more than two independent groups, and the Pearson correlation test for comparing two numerical variables. A statistical significance level was set at p<0.05.

RESULTS

Of the participants, 64.2% were female (n=154) and 35.8% were male (n=86), with an average age of 45.04±10.85. The average age of the patients receiving care was 78.40±14.94. While the average total score of the participants from CSS-12 was 22.36±11.63, the average score they received from HAI was 17.69±11.54. The socio-demographic data of the participants and the comparison of these data with the CSS-12 and HAI scores are presented in Table 1.

Tabl	e 1 . Demograp	hic data o	f the participants and	l comparison of th	e data with t	he scores t	hev received fr	om the CSS-12 and HAI scales.
			and participante and					

		Ν	CSS-12*	Р	HAI**	Р
Gender	Female	154	24.20±12.33	<0.001	18.14±11.54	0.351
	Male	86	19.06±9.67		16.87±	
Marital status	Married	187	21.58±11.32	0.018	18.06±11.74	0.061
	Single	40	26.90±12.17		14.25±9.08	
	Widowed	13	19.62±11.75		22.92±13.27	
Marital status of the patient receiving care	Married	86	16.10±11.48	0.284	23.22±11.36	0.577
	Single	12	18.33±9.75		23.83±12.11	
	Widowed	142	18.55±11.54		21.71±11.78	
Educational Status	Illiterate	4	20.75±17.50	0.130	14.00±8.83	0.273
	Primary school	95	20.56±10.09		18.55±11.13	
	High school	73	22.32±12.32		18.56±12.33	
	University and above	68	25.01±12.28		15.76±11.31	
Educational status of the cared patient	Illiterate	112	18.35±11.27	0.852	20.82±10.96	0.055
	Primary school	113	17.21±12.26		22.96±11.87	
	High school	10	16.70±7.64		29.10±14.56	
	University and above	5	15.60±8.05		29.60±8.01	
Relationship with the cared-for patient	Daughter - son	137	21.81±11.67	0.884	18.09±11.39	0.688
	Mother - Father	5	24.00±12.39		17.00±7.71	
	Brother-Sister	6	23.00±14.00		21.17±12.22	
	Bride-groom	41	23.90±12.35		19.20±14.07	
	Grandson-nephew	37	22.14±10.54		15.22±9.93	
	Other	14	22.93±12.25		14.64±9.51	
Presence of chronic disease	Yes	89	21.00±11.52	0.112	19.84±11.69	0.016
	No	151	23.16±11.65		16.42±11.29	
Psychiatric medication	Yes	19	21.79±11.50	0.860	26.95±12.04	<0.001
	No	Inite 11.1 11.1 11.1 Iale 86 19.06±9.67 Iarried 187 21.58±11.32 0.018 ingle 40 26.90±12.17 11.1 Vidowed 13 19.62±11.75 0.130 ingle 12 18.33±9.75 11.3 Vidowed 142 18.55±11.54 0.130 rimary school 95 20.56±10.09 11.3 rimary school 73 22.32±12.32 0.130 niversity and above 68 25.01±12.28 11.3 rimary school 10 16.70±7.64 11.4 rintersity and above 5 15.60±8.05 11.5 niversity and above 5 24.00±12.39 11.5 rother - Father 5 24.00±12.39 11.5 rother - Sister 6 23.00±14.00 11.5 rinde-groom 11	16.53±10.99			
	I do not want to mention	7	25.43±15.44		27.86±11.78	

*CSS-12: Cyberchondria Severity Scale Short Form

**HAI: Health Anxiety Scale

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Participants allocated 2.03 ± 1.63 hours (min=0, max=9) for personal time during the day, with an average of 0.48 ± 0.68 hours (min=0, max=5) dedicated to online health research. The durations for caregiving, personal time, and online browsing by the participants are detailed in Table 2. The responses given by participants to each item on the CSS-12 scale and the average scores are depicted in Figure 1. A significant positive correlation was identified between CSS-12 and HAI (r=0.404, p<0.001). The results of the Pearson correlation analysis between caregiving duration, caregiving difficulty, time allocated for oneself and online, time spent on online health research, and scores from the HAI and CSS-12 are provided in Figure 2.

Table 2. Participants' caregiving, self-time, and browsing time.

	Mean	Ss	Min*.	Max.
How many days a week do you come to the patient receiving care? (days)	6.01	1.59	2	7
How many hours per day do you allocate to the patient receiving care? (hours)	8.48	4.93	1	24
How long have you been caring for the patient? (months)	60.40	60.55	1	408
If you rate your patient's care hardship on a low of 1 and a high of 10. how many points will you give?	7.85	2.09	1	10
How much time do you spend on yourself during the day? (hour)	2.03	1.63	0	9
How much time do you spend online daily? (hours)	1.5	1.42	0	9
How much time do you spend on health topics online daily? (hours)	0.48	0.68	0	5

*. Under 30 minute is considered as "0".

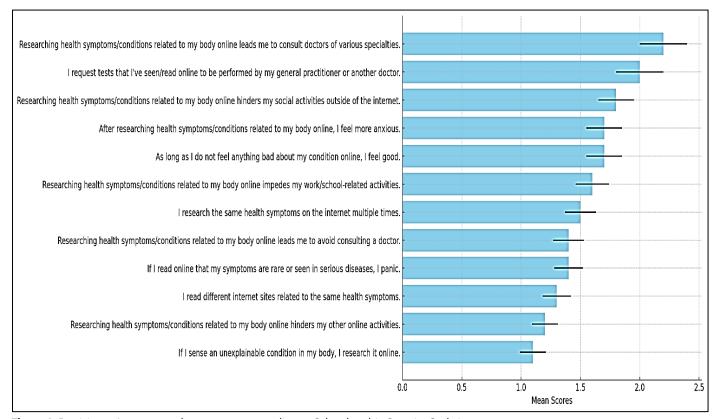


Figure 1. Participants' answers and mean scores according to Cyberchondria Severity Scale items

	Duration allocated for daily patient care	Perceived care difficulty	Duration of care provided (months)	Daily personal time	Time spent on the internet	Time allocated for health research	CSS-12 score	HAI score	
Duration allocated for daily patient care	1.000	0.263	0.140	-0.285	-0.222	-0.068	-0.093	0.013	1 .
Perceived care difficulty	0.263	1.000	0.128	-0.308	-0.211	-0.100	-0.026	0.136	- 0.
Duration of care provided (months)	0.140	0.128	1.000	-0.167	-0.169	-0.076	0.018	0.076	0.
Daily personal time	-0.285	-0.308	-0.167	1.000	0.426	0.167	0.143	-0.119	- 0
Time spent on the internet	-0.222	-0.211	-0.169	0.426	1.000	0.491	0.297	-0.052	
Time allocated for health research	-0.068	-0.100	-0.076	0.167	0.491	1.000	0.609	0.229	0
CSS-12 score	-0.093	-0.026	0.018	0.143	0.297	0.609	1.000	0.404	-0
HAI score	0.013	0.136	0.076	-0.119	-0.052	0.229	0.404	1.000	-1.

Figure 2. Care time, difficulty, time allocated to self and internet, HAI and CSS-12 scale scores Pearson correlation analysis results. *CSS-12: Cyberchondria Severity Scale Short Form

**HAI: Health Anxiety Scale

DISCUSSION

This study, focusing on the relationship between cyberchondria levels and health anxiety among relatives of patients receiving home healthcare, introduces a novel perspective to the literature. The findings reveal a significant positive correlation between the Health Anxiety Inventory scores and the Cyberchondria Severity Scale scores. This result illuminates the dynamics between cyberchondria and health anxiety, shedding light on their interaction and potential implications for individuals' psychological well-being. In this discussion section, the findings will be evaluated in light of existing literature, and potential implications for clinical practice and policymaking will be addressed.

Based on the observed data, the time participants allocate for themselves daily appears limited. Moreover, they spend much of this limited time online, dedicating about a third to health-related research. The findings indicate an increase in health anxiety and cyberchondria levels as the time spent on online health research increases. These results align with the existing literature. Starcevic (2017) defined cyberchondria as the repetitive use of the internet to search for health-related information, which can exacerbate health anxiety (6). This is consistent with our findings that as participants spend more time researching health online, their levels of health anxiety and cyberchondria increase. Jungmann et al. (2020) also highlighted that internet use for health-related purposes is a primary factor in perpetuating and escalating emotional distress (16). This parallels our findings, where participants spend a significant portion of their personal time online, with a substantial part dedicated to health research. Furthermore, Singh and Brown (2016) noted that searching for disease information online can intensify anxiety, especially in individuals already concerned about their health. This supports our findings regarding the potential exacerbation of health anxiety due to online health information searches (17).

The study's outcomes suggest that socio-demographic variables such as marital status, educational background, and the relationship with the patient receiving care do not have a pronounced effect on health anxiety and cyberchondria. However, a notable higher level of cyberchondria was observed among female participants. Regarding health anxiety, while females scored higher than males, the difference was not statistically significant. This observation aligns with most studies in the literature (18), though some reports suggest gender influences health anxiety (19). Further research is warranted to understand better the role of gender in health anxiety and cyberchondria.

Individuals with chronic diseases or those taking psychiatric medications exhibited significantly elevated levels of health anxiety. This could reflect the constant health concerns these individuals harbour. Such heightened anxiety could adversely impact their access and utilisation of healthcare services, necessitating the development of tailored intervention strategies for this group.

Regarding cyberchondria levels, no significant difference was observed among participants with chronic diseases or those on psychiatric medications. This contrasts with some literature where individuals with chronic diseases or those on psychiatric medications exhibited higher cyberchondria levels (20). The discrepancy might be attributed to the majority of our sample being familiar with internet use and being able to control their online health information-seeking behaviours. Additionally, individuals with chronic diseases or those on psychiatric medications might prefer home healthcare services, providing easy access to health information without using the internet.

When analysing scores from the Cyberchondria Severity Scale, the item "I feel good unless I see something bad about my condition online" received the highest score. This item reflects the emotional dimension of participants' online health information-seeking behaviours, suggesting that they might use this behaviour as a coping strategy. This aligns with the cyberchondria model in the literature where individuals search online for health information to alleviate health-related concerns (6). However, this behaviour can paradoxically amplify these concerns, pushing individuals to seek more information.

On the other hand, the lowest score was given to the statement, "Searching for symptoms/body conditions online hinders my work/school-related activities," suggesting that online health information-seeking does not significantly disrupt participants' daily lives. This could imply that individuals prioritise other daily activities over online health information-seeking. This observation is supported by a meta-analysis by Jian Wang et al. (2019), which found that online health information-seeking varies based on individuals' health beliefs and attitudes (21).

The findings that both health anxiety and cyberchondria levels significantly increase with more time spent on online health research align with existing literature (6,22). Online health research can serve as a resource individuals turn to for alleviating health concerns. However, this research can also amplify these concerns, creating a vicious cycle between health anxiety and cyberchondria.

The moderate statistically significant relationship between health anxiety and cyberchondria levels is consistent with literature suggesting that while cyberchondria overlaps with health anxiety, it is also distinguishable (23). This supports the notion that cyberchondria might be a manifestation of health anxiety or that these two phenomena interact.

The nature of the relationship between health anxiety and cyberchondria remains to be fully elucidated. However, in light of these findings, further research is needed to understand the nature, interaction, and potential overlaps between these two phenomena. Additionally, a deeper exploration of individuals' online health information-seeking behaviour and its impact on these phenomena is crucial.

Limitations

Our study has several limitations. Notably, the scales were administered to caregivers rather than the patients themselves, which could impact the applicability of results to patients' experiences. The cross-sectional design of the study limits our ability to draw causal inferences. The findings, derived from a specific regional context, may not be generalizable to other populations. Potential response bias due to the sensitive nature of the topics and the absence of qualitative data to enrich our understanding of the caregivers' experiences further limits the scope of our conclusions. Acknowledging these limitations is essential for interpreting our study's findings and for informing future research directions in this field. Hence, further studies conducted across a broader population, using various interview techniques in multi-centre settings, are needed.

CONCLUSION

This study contributes to the literature by examining the relationship between cyberchondria levels and health anxiety among relatives of patients receiving home healthcare. The findings reveal a significant positive relationship between cyberchondria and health anxiety. Moreover, the relationship between these two phenomena strengthens with increased time spent on online health research.

The study's outcomes can aid in better understanding the dynamics between cyberchondria and health anxiety, illuminating their interaction and potential implications for individuals' psychological well-being. Additionally, these results provide valuable insights for healthcare professionals, especially when considering interventions for relatives of patients receiving home healthcare. Lastly, this study emphasises the need for further research to understand the nature, interaction, and potential overlaps between cyberchondria and health anxiety. Such research can contribute to developing effective interventions to support individuals' psychological well-being and mitigate the interaction between these two phenomena.

DECLARATIONS

Ethical considerations: This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Erzincan Binali Yıldırım University on 30.03.2023, with the decision number 2023/07-5. All participants were informed about the purpose of the research and provided their voluntary consent before participation.

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Conflict of Interest Statement: There are no potential conflicts of interest to declare.

Data Availability Statement: The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

REFERENCES

- Landers S, Madigan E, Leff B, Rosati RJ, McCann BA, Hornbake R, et al. The future of home health care: a strategic framework for optimizing value. Home health care management practice. 2016;28(4):262-78.
- Melin-Johansson C, Ödling G, Axelsson B, Danielson E. The meaning of quality of life: Narrations by patients with incurable cancer in palliative home care. Palliative supportive care. 2008;6(3):231-8.
- Arsenakis S, Chatton A, Penzenstadler L, Billieux J, Berle D, Starcevic V, et al. Unveiling the relationships between cyberchondria and psychopathological symptoms. 2021;143:254-61.
- Soyler S, Cavmak S, Cavmak D. The impact of health anxiety and distrust in the healthcare system on cyberchondria: a cross-sectional study. British Journal of Healthcare Management. 2023;29(2):1-8.
- Afrin R, Prybutok G. Insights into the antecedents of cyberchondria: a perspective from the USA. Health Promotion International. 2022;37(4):daac108.
- Starcevic V, Baggio S, Berle D, Khazaal Y, Viswasam K. Cyberchondria and its relationships with related constructs: A network analysis. Psychiatric quarterly. 2019;90:491-505.
- Starcevic V, Berle D, Arnáez S. Recent insights into cyberchondria. Current Psychiatry Reports. 2020;22:1-8.
- López-Solà C, Bui M, Hopper JL, Fontenelle LF, Davey CG, Pantelis C, et al. Predictors and consequences of health anxiety symptoms: a novel twin modeling study. Acta Psychiatrica Scandinavica. 2018;137(3):241-51.
- Alshraifeen A, Al-Rawashdeh S, Alnuaimi K, Tawalbeh L, Ashour A. Depression and anxiety predicted quality of life in dyads of people

receiving hemodialysis treatment and their family caregivers. Current Psychology. 2023:1-13.

- Tyrer P, Cooper S, Tyrer H, Wang D, Bassett P. Increase in the prevalence of health anxiety in medical clinics: possible cyberchondria. International Journal of Social Psychiatry. 2019;65(7-8):566-9.
- McElroy E, Kearney M, Touhey J, Evans J, Cooke Y, Shevlin M. The CSS-12: Development and Validation of a Short-Form Version of the Cyberchondria Severity Scale. Cyberpsychology, behavior and social networking. 2019;22(5):330-5.
- Söyler S, Biçer İ, Çavmak D. Cyberchondria Severity Scale Short Form (CSS-12) Validity and Reliability Study. Davranışsal Boyutları ile Sağlık 2021.
- Selvi Y, Turan S, Sayin A, Boysan M, Kandeğer A. The Cyberchondria Severity Scale (CSS): Validity and Reliability Study of the Turkish Version. Sleep and Hypnosis - International Journal. 2018;20:241-6.
- Salkovskis PM, Rimes KA, Warwick HM, Clark DM. The Health Anxiety Inventory: development and validation of scales for the measurement of health anxiety and hypochondriasis. Psychological medicine. 2002;32(5):843-53.
- Aydemir Ö, Kirpinar I, Tülay S, Uykur B, Cengisiz C. Reliability and validity of the Turkish version of the health anxiety inventory. Nöro Psikiyatri Arşivi. 2013;50(4):325.
- Jungmann SM, Brand S, Kolb J, Witthöft M. Do Dr. Google and health apps have (comparable) side effects? An experimental study. Clinical Psychological Science. 2020;8(2):306-17.
- Singh K, Brown RJ. From headache to tumour: An examination of health anxiety, health-related Internet use and 'query escalation'. Journal of Health Psychology. 2016;21(9):2008-20.
- Gaus V, Kiep H, Holtkamp M, Burkert S, Kendel F. Gender differences in depression, but not in anxiety in people with epilepsy. Seizure. 2015;32:37-42.
- MacSwain KLH, Sherry SB, Stewart SH, Watt MC, Hadjistavropoulos HD, Graham AR. Gender differences in health anxiety: An investigation of the interpersonal model of health anxiety. Personality Individual Differences. 2009;47(8):938-43.
- Kurcer MA, Erdogan Z, Cakir Kardes V. The effect of the COVID-19 pandemic on health anxiety and cyberchondria levels of university students. Perspectives in psychiatric care. 2022;58(1):132-40.
- Wang J, Xiu G, Shahzad F. Exploring the determinants of online health information-seeking behavior using a meta-analytic approach. Sustainability. 2019;11(17):4604.
- Muse K, McManus F, Leung C, Meghreblian B, Williams JMG. Cyberchondriasis: fact or fiction? A preliminary examination of the relationship between health anxiety and searching for health information on the Internet. Journal of anxiety disorders. 2012;26(1):189-96.
- Menon V, Kar SK, Tripathi A, Nebhinani N, Varadharajan N. Cyberchondria: conceptual relation with health anxiety, assessment, management and prevention. Asian Journal of Psychiatry. 2020;53:102225.

Dietary Supplementation with Macronutrients and Vitamins to Prevent and

Slow the Progression of Alzheimer's Disease: A Comprehensive Review

Murat KÖSEDAĞ^{1*}

Review

¹ Department of Biochemistry, Atatürk University, Faculty of Pharmacy, Erzurum, Türkiye

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*Corresponding author: Murat KÖSEDAĞ, Department of Biochemistry, Atatürk University, Faculty of Pharmacy, Erzurum, Türkiye. E-mail: <u>kosedagmurat08@gmail.com</u> Cite This Article as: Kösedağ M. Dietary Supplementation with Macronutrients and Vitamins to Prevent and Slow the Progression of Alzheimer's Disease: A Comprehensive Review. Essentials Frontline Med J. 2025:2(1); 14-18.

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ABSTRACT

Alois Alzheimer, in 1901, first described Alzheimer's Disease, a progressive neurological disorder that stands as the leading cause of dementia. Its prevalence is alarmingly escalating globally, correlating with increased life expectancies. Current treatments for Alzheimer's Disease are limited, with available medications being expensive and often accompanied by adverse health effects. This necessitates the exploration of natural, readily accessible, and practical therapeutic approaches to both prevent and decelerate the disease's progression. Dietary awareness emerges as a significant natural intervention. Recent research has increasingly focused on the link between nutrition and Alzheimer's Disease, demonstrating a strong correlation between dietary patterns and the disease's development. A well-balanced, sustainable diet, rich in essential macronutrients (proteins, carbohydrates, and fats) and supplemented with vital vitamins, holds potential in preventing Alzheimer's onset in healthy individuals and significantly slowing its advancement in diagnosed patients. This review aims to analyze current research on the impact of macronutrients and vitamins in mitigating Alzheimer's Disease.

Keywords: Alzheimer's Disease, nutrition, macronutrients, prevention, vitamins

INTRODUCTION

In 1901, the German psychiatrist and neuropathologist, Alois Alzheimer, encountered Auguste Deter, a 51-year-old patient exhibiting behavioral anomalies impacting daily life, persistent paranoia, severe memory impairment, and dementia symptoms. Intrigued, Alzheimer closely monitored the patient's symptom progression until her death in 1906. Hypothesizing that these symptoms stemmed from physiological and biochemical brain alterations, Alzheimer sought to examine Deter's brain postmortem. Obtaining approval, he conducted detailed microscopic analyses, revealing significant brain changes, including amyloid plaques and neurofibrillary tangles, indicative of pathological signs. In 1906, he published his findings on these observations. Dr. Emil Kraepelin, advocating for pathological bases of mental disorders, embraced Alzheimer's findings, naming the condition 'Alzheimer's' (1-4).

Alzheimer's Disease (AD), the most prevalent cause of dementia, is a neurological condition primarily resulting from the accumulation of abnormally folded amyloid beta protein in the brain, classifying it as a proteopathy (5, 6). The disorder manifests through various histopathological, molecular, and biochemical abnormalities, such as amyloid beta protein deposits, neuronal loss, neurofibrillary tangles, dystrophic neurites, increased pro-death gene activation, impaired energy metabolism, mitochondrial dysfunction, chronic oxidative stress, and DNA damage (7). These abnormalities also reflect brain insulin resistance and deficiency, with biochemical consequences overlapping with type 1 and type 2 diabetes. Hence, recent studies emphasize insulin resistance and glucose metabolism impairment in AD pathogenesis, suggesting its reclassification as "type 3 diabetes" (8, 9).

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AD, a progressive neurodegenerative condition marked by cognitive decline, lacks a definitive cure, and its medications often induce side effects (10). Consequently, a tailored daily diet and supplementary intake become crucial for AD patients. Dietary adjustments and conscious nutrition programs can modify the disease's trajectory, slow its progression, and enhance patient quality of life (11, 12). This review explores the relationship between AD and diet, focusing on vitamin and macronutrient programming, based on current literature.

PROTEIN, CARBOHYDRATES, AND FATS IN ALZHEIMER'S DISEASE

The impact of diet and lifestyle on cognitive function and neurodegenerative diseases has increasingly been examined, particularly in the last three decades. Studies on macronutrient (carbohydrate, fat, and protein) effects on AD development and progression have intensified (13). Cross-sectional and epidemiological studies highlight nutritional parameters' influence on human cognition (14). Chronic conditions like type 2 diabetes, insulin resistance, obesity, cardiovascular disease, and hypertension are dementia risk factors (15). Similarly, dietary patterns contribute to cognitive impairment and AD risk. Optimal macronutrient balance through diet enhances cognitive function, while poor dietary habits can lead to metabolic disorders and chronic diseases (16).

Recent studies indicates that excessive carbohydrate intake, especially fructose, may contribute to AD development. Elevated plasma glucose and monosaccharides can cause glycation of fat, cholesterol, and oxygen transport proteins, altering their structure. This leads to neuronal cholesterol deficiency, impairing nerve cell function. Over time, this results in disrupted glutamate signaling, increased oxidative damage, mitochondrial and lysosomal dysfunction, and higher microbial infection risk, leading to apoptosis. These metabolic disorders can significantly contribute to neurodegenerative diseases, including Alzheimer's (17).

A study at the University of Kansas Medical Center observed brain amyloid plaque changes in cognitively normal older adults with high-glycemic diets. Results showed increased amyloid deposition in temporoparietal cortex regions in adults with high-carbohydrate diets, especially those with high amyloid status, over a year (18). Animal studies have shown that chronic high-calorie diets, rich in sugar and saturated fatty acids, can induce brain damage, triggering inflammation in areas like the hypothalamus, hippocampus, and frontal cortex, increasing oxidative stress, and causing metabolic disturbances, reduced dendritic spines, and memory loss (19).

The ketogenic diet, high in fat, moderate in protein, and low in carbohydrates, has been used since 500 BC, notably for epilepsy (20). It remains a natural treatment for drug-resistant epilepsy (21-23). Clinical studies show long-term therapeutic benefits for

epilepsy patients on ketogenic diets (24-26). Recent research suggests it can reduce anti-seizure medication use (27). A pilot study on AD patients showed slight cognitive improvements after 12 weeks on a ketogenic diet (28). Animal studies indicate potential symptomatic and disease-modifying effects in neurodegenerative disorders, including AD and Parkinson's, and protective effects in brain injury and stroke (29-32).

The Mediterranean Diet, introduced by Ancel Keys, emphasizes unrefined grains, fruits, vegetables, legumes, olive oil, moderate fish and poultry consumption, and limited dairy and red meat (33-36). A study of 512 patients found that a Mediterranean-like diet correlated with greater medial-temporal gray matter volume, better memory, and reduced amyloid and p-tau pathology (37). A large cohort study showed high adherence to the Mediterranean diet was associated with better cognitive performance and reduced memory decline (38). Overall, a diet low in high-glycemic carbohydrates, rich in healthy fats, and balanced in animal and vegetable proteins may be beneficial for brain health.

VITAMINS AND ALZHEIMER'S DISEASE

Vitamin A derivatives, crucial in brain cellular processes, show decreased serum/plasma concentrations in AD (39-41). Retinoid deficiency may predispose to AD by increasing cerebral amyloid β accumulation (42). Studies on transgenic mice showed that all-trans retinoic acid, a vitamin A metabolite, reduced brain amyloid beta accumulation and tau phosphorylation, improved spatial learning, and decreased neuronal degeneration (43).

A study of elderly men showed that B vitamin supplements reduced Aβ40 protein increase, suggesting a potential role in AD prevention (44). Meta-analyses indicate that vitamin B supplementation slows cognitive decline, especially with early and long-term intervention, and that folate intake is associated with reduced dementia incidence (45). Folic acid and vitamin B12 supplements improved cognitive performance and reduced inflammation in elderly patients with mild cognitive impairment (46). These supplements also prevented AD-like memory deficits (47). Low vitamin B12 intake was associated with accelerated cognitive decline and affected DNA methylation of redox-related genes (48).

Vitamin C deficiency can disrupt neurotransmitter synthesis, increase oxidative stress, and promote amyloid beta plaque accumulation, contributing to AD neurodegeneration. Metaanalyses suggest vitamin C deficiency plays a role in AD progression, and supplementation may be beneficial (49). Vitamin

C attenuates neuroinflammation and inhibits amyloid beta peptide accumulation (50). It may also have preventive and therapeutic effects on mental illnesses like depression, schizophrenia, and anxiety (51).

Vitamin D, a steroid hormone, influences calcium-phosphorus metabolism, cardiovascular health, immune responses, and brain function (52-55). Low vitamin D levels are associated with neurodegeneration and cognitive decline (56). Vitamin D affects neurotransmitter levels, regulates neurotrophic factors, and aids in amyloid beta peptide clearance (57-59). It may also help clear amyloid plaques through innate immune cells and alleviate cognitive deficits (60). Vitamin E, an antioxidant, may protect cognitive health by scavenging free radicals (61, 62). Low vitamin E levels increase AD risk, and a vitamin E-rich diet may slow AD progression (63).

Vitamin K, crucial for sphingolipid metabolism, affects brain cell proliferation, differentiation, and survival (64). It also impacts Gas-6 protein and protein S molecules, vital for cognitive function (65). Vitamin K deficiency is associated with cognitive impairment (66). Vitamin K2 may prevent apoptosis, oxidative stress, and microglial activation in neuronal cells, showing promise against AD (66).

CONCLUSION

AD is a progressive neurodegenerative disorder that affects millions of individuals globally and continues to increase in prevalence due to the aging population. Despite extensive research, no definitive cure for AD currently exists. Moreover, the pharmacological treatments available are associated with numerous health complications, primarily due to their adverse side effects and high cost, which significantly limit their long-term applicability and effectiveness. In light of these limitations, there is a growing interest in natural and non-pharmacological approaches aimed at preventing or decelerating the progression of the disease. Among these, conscious and evidence-based nutritional strategies have garnered particular attention. Emerging research increasingly supports a strong correlation between dietary habits and the onset and progression of AD. Numerous findings suggest that this condition is intimately linked to long-term nutritional behaviors. A well-structured and sustainable diet-balanced in macronutrients (proteins, carbohydrates, and fats) and adequately supplemented with essential vitamins and micronutrients-has the potential not only to delay the onset of AD in healthy individuals but also to significantly slow its progression in those already affected. Nevertheless, it must be acknowledged that further scientific investigation is required to elucidate the precise mechanisms by which diet influences AD pathophysiology. As the etiopathogenesis of Alzheimer's Disease remains partially understood, more studies are essential to validate existing data and to explore new dietary intervention strategies.

In conclusion, while pharmacological treatments remain integral to the current clinical management of AD, nutrition-based approaches offer a promising complementary avenue that is both accessible and low-risk. Continued interdisciplinary research is imperative to better define the role of diet in the prevention and management of Alzheimer's Disease and to develop standardized nutritional guidelines that can be implemented in clinical and public health contexts.

DECLARATIONS

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REFERENCES

- Parle M, Balhara P, Kaura S. The mystery and history of Alzheimer's disease. Int J Pharm Sci & Res. 2023;14:3231-7.
- Cipriani G, Dolciotti C, Picchi L, Bonuccelli U. Alzheimer and his disease: a brief history. Neurological Sciences. 2011;32:275-9.
- 3. Nitrini R. The past, present and future of Alzheimer's disease-part 1: the past. Arguivos de Neuro-psiguiatria. 2023;81(12):1070-6.
- 4. Bick KL. The early story of Alzheimer's disease. (No Title). 1987.
- Casaletto KB, Nichols E, Aslanyan V, Simone SM, Rabin JS, La Joie R, et al. Sex-specific effects of microglial activation on Alzheimer's disease proteinopathy in older adults. Brain. 2022;145(10):3536-45.
- Sadigh-Eteghad S, Sabermarouf B, Majdi A, Talebi M, Farhoudi M, Mahmoudi J. Amyloid-Beta: A Crucial Factor in Alzheimer's Disease. Medical Principles and Practice. 2014;24(1):1-10.
- De la Monte SM, Wands JR. Alzheimer's disease is type 3 diabetes evidence reviewed. Journal of diabetes science and technology. 2008;2(6):1101-13.
- Kciuk M, Kruczkowska W, Gałęziewska J, Wanke K, Kałuzińska-Kołat Ż, Aleksandrowicz M, et al. Alzheimer's Disease as Type 3 Diabetes: Understanding the Link and Implications. International Journal of Molecular Sciences. 2024;25(22):11955.
- De la Monte SM. Type 3 diabetes is sporadic Alzheimer's disease: Minireview. European Neuropsychopharmacology. 2014;24(12):1954-60.

- Casey DA, Antimisiaris D, O'Brien J. Drugs for Alzheimer's disease: are they effective? P & T : a peer-reviewed journal for formulary management. 2010;35(4):208-11.
- Pistollato F, Iglesias RC, Ruiz R, Aparicio S, Crespo J, Lopez LD, et al. Nutritional patterns associated with the maintenance of neurocognitive functions and the risk of dementia and Alzheimer's disease: A focus on human studies. Pharmacological Research. 2018;131:32-43.
- Dauncey MJ. Nutrition, the brain and cognitive decline: insights from epigenetics. European Journal of Clinical Nutrition. 2014;68(11):1179-85.
- Hirschberg S, Gisevius B, Duscha A, Haghikia A. Implications of Diet and The Gut Microbiome in Neuroinflammatory and Neurodegenerative Diseases. International Journal of Molecular Sciences. 2019;20(12):3109.
- Popa-Wagner A, Dumitrascu DI, Capitanescu B, Petcu EB, Surugiu R, Fang W-H, et al. Dietary habits, lifestyle factors and neurodegenerative diseases. Neural Regeneration Research. 2020;15(3).
- Barone E, Di Domenico F, Perluigi M, Butterfield DA. The interplay among oxidative stress, brain insulin resistance and AMPK dysfunction contribute to neurodegeneration in type 2 diabetes and Alzheimer disease. Free Radical Biology and Medicine. 2021;176:16-33.
- Binosha Fernando WMAD, Gupta VB, Jayasena V, Brennan CS, Martins RN. Carbohydrate and Protein Metabolism: Influences on Cognition and Alzheimer's Disease. Neurodegeneration and Alzheimer's Disease2019. p. 149-87.
- Seneff S, Wainwright G, Mascitelli L. Nutrition and Alzheimer's disease: The detrimental role of a high carbohydrate diet. European Journal of Internal Medicine. 2011;22(2):134-40.
- Taylor MK, Sullivan DK, Morris JK, Vidoni ED, Honea RA, Mahnken JD, et al. High glycemic diet is related to brain amyloid accumulation over one year in preclinical Alzheimer's disease. Frontiers in Nutrition. 2021;8:741534.
- Fuentes E, Venegas B, Muñoz-Arenas G, Moran C, Vazquez-Roque RA, Flores G, et al. High-carbohydrate and fat diet consumption causes metabolic deterioration, neuronal damage, and loss of recognition memory in rats. Journal of Chemical Neuroanatomy. 2023;129:102237.
- O'Neill B, Raggi P. The ketogenic diet: Pros and cons. Atherosclerosis. 2020;292:119-26.
- Zarnowska IM. Therapeutic Use of the Ketogenic Diet in Refractory Epilepsy: What We Know and What Still Needs to Be Learned. Nutrients. 2020;12(9):2616.
- Sondhi V, Sharma S. Non-Pharmacological and Non-Surgical Treatment of Refractory Childhood Epilepsy. The Indian Journal of Pediatrics. 2020;87(12):1062-9.
- Schoeler NE, Leu C, Balestrini S, Mudge JM, Steward CA, Frankish A, et al. Genome-wide association study: Exploring the genetic basis for responsiveness to ketogenic dietary therapies for drug-resistant epilepsy. Epilepsia. 2018;59(8):1557-66.

- Kverneland M, Molteberg E, Haavardsholm KC, Pedersen S, Ramm-Pettersen A, Nakken KO. Diettbehandling av epilepsi. Tidsskrift for Den norske legeforening. 2017.
- Mayung C. Efektivitas Diet Ketogenik dalam Penurunan Frekuensi Kejang pada Anak Dengan Epilepsi Resisten Obat. Termometer: Jurnal Ilmiah Ilmu Kesehatan dan Kedokteran. 2023;1(1):43-55.
- Saputra DH. Peran Diet Ketogenik dalam Tata Laksana Epilepsi. Cermin Dunia Kedokteran. 2022;49(11):629-34.
- He F, Ye L, Wang L, Zhou J, Shao X, Miao P, et al. Ketogenic diet therapy leads to antiseizure medication reduction in children and adults with drug-resistant epilepsy. CNS Neuroscience & Therapeutics. 2024;30(7):e14854.
- Taylor MK, Sullivan DK, Mahnken JD, Burns JM, Swerdlow RH. Feasibility and efficacy data from a ketogenic diet intervention in Alzheimer's disease. Alzheimer's & Dementia: Translational Research & Clinical Interventions. 2018;4:28-36.
- Lusardi TA, Akula KK, Coffman SQ, Ruskin DN, Masino SA, Boison D. Ketogenic diet prevents epileptogenesis and disease progression in adult mice and rats. Neuropharmacology. 2015;99:500-9.
- Shaafi S, Najmi S, Aliasgharpour H, Mahmoudi J, Sadigh-Etemad S, Farhoudi M, et al. The efficacy of the ketogenic diet on motor functions in Parkinson's disease: A rat model. Iranian journal of neurology. 2016;15(2):63-9.
- Yüzgüleç M, Korkmaz ND, Elibol B. Effects of Ketogenic Diet on Rat Model of Sporadic Alzheimer's Disease. Bezmialem Science. 2022;10.
- Lin C, Wang S, Xie J, Zhu J, Xu J, Liu K, et al. Ketogenic diet and β-Hydroxybutyrate alleviate ischemic brain injury in mice via an IRAKMdependent pathway. European Journal of Pharmacology. 2023;955:175933.
- Keys A, Mienotti A, Karvonen MJ, Aravanis C, Blackburn H, Buzina R, et al. The diet and 15-year death rate in the seven countries study. American journal of epidemiology. 1986;124(6):903-15.
- Bach-Faig A, Berry EM, Lairon D, Reguant J, Trichopoulou A, Dernini S, et al. Mediterranean diet pyramid today. Science and cultural updates. Public Health Nutrition. 2011;14(12A):2274-84.
- Guasch-Ferré M, Willett WC. The Mediterranean diet and health: a comprehensive overview. Journal of Internal Medicine. 2021;290(3):549-66.
- Muscogiuri G, Verde L, Sulu C, Katsiki N, Hassapidou M, Frias-Toral E, et al. Mediterranean Diet and Obesity-related Disorders: What is the Evidence? Current Obesity Reports. 2022;11(4):287-304.
- Ballarini T, Melo van Lent D, Brunner J, Schröder A, Wolfsgruber S, Altenstein S, et al. Mediterranean Diet, Alzheimer Disease Biomarkers, and Brain Atrophy in Old Age. Neurology. 2021;96(24):e2920-e32.
- Moustafa B, Trifan G, Isasi CR, Lipton RB, Sotres-Alvarez D, Cai J, et al. Association of Mediterranean Diet With Cognitive Decline Among Diverse Hispanic or Latino Adults From the Hispanic Community Health Study/Study of Latinos. JAMA Network Open. 2022;5(7):e2221982-e.
- Lane MA, Bailey SJ. Role of retinoid signalling in the adult brain. Progress in neurobiology. 2005;75(4):275-93.

- Bourdel-Marchasson I, Delmas-Beauvieux MC, Peuchant E, Richard-Harston S, Decamps A, Reignier B, et al. Antioxidant defences and oxidative stress markers in erythrocytes and plasma from normally nourished elderly Alzheimer patients. Age and Ageing. 2001;30(3):235-41.
- Rinaldi P, Polidori MC, Metastasio A, Mariani E, Mattioli P, Cherubini A, et al. Plasma antioxidants are similarly depleted in mild cognitive impairment and in Alzheimer's disease. Neurobiology of Aging. 2003;24(7):915-9.
- 42. Corcoran JPT, So PL, Maden M. Disruption of the retinoid signalling pathway causes a deposition of amyloid β in the adult rat brain. European Journal of Neuroscience. 2004;20(4):896-902.
- Ding Y, Qiao A, Wang Z, Goodwin JS, Lee E-S, Block ML, et al. Retinoic acid attenuates β-amyloid deposition and rescues memory deficits in an Alzheimer's disease transgenic mouse model. Journal of Neuroscience. 2008;28(45):11622-34.
- Flicker L, Martins RN, Thomas J, Acres J, Taddei K, Vasikaran SD, et al. B-vitamins reduce plasma levels of beta amyloid. Neurobiology of Aging. 2008;29(2):303-5.
- Wang Z, Zhu W, Xing Y, Jia J, Tang Y. B vitamins and prevention of cognitive decline and incident dementia: a systematic review and metaanalysis. Nutrition Reviews. 2021;80(4):931-49.
- 46. Ma F, Zhou X, Li Q, Zhao J, Song A, An P, et al. Effects of folic acid and vitamin B12, alone and in combination on cognitive function and inflammatory factors in the elderly with mild cognitive impairment: a single-blind experimental design. Current Alzheimer Research. 2019;16(7):622-32.
- Guo J, Ni S, Li Q, Wang J-Z, Yang Y. Folate/Vitamin B Alleviates Hyperhomocysteinemia-Induced Alzheimer-Like Pathologies in Rat Retina. Neuroscience Bulletin. 2019;35(2):325-35.
- An Y, Feng L, Zhang X, Wang Y, Wang Y, Tao L, et al. Dietary intakes and biomarker patterns of folate, vitamin B 6, and vitamin B 12 can be associated with cognitive impairment by hypermethylation of redoxrelated genes NUDT15 and TXNRD1. Clinical epigenetics. 2019;11:1-19.
- Hamid M, Mansoor S, Amber S, Zahid S. A quantitative meta-analysis of vitamin C in the pathophysiology of Alzheimer's disease. Frontiers in aging neuroscience. 2022;14:970263.
- Monacelli F, Acquarone E, Giannotti C, Borghi R, Nencioni A. Vitamin C, Aging and Alzheimer's Disease. Nutrients. 2017;9(7):670.
- Han Q-q, Shen T-t, Wang F, Wu P-f, Chen J-g. Preventive and Therapeutic Potential of Vitamin C in Mental Disorders. Current Medical Science. 2018;38(1):1-10.
- Balcı C, Toktaş N. D Vitamini Sentezi, Metabolizmasi Ve Sağlık Üzerine Etkileri. Gazi Sağlık Bilimleri Dergisi. 2021;6(1):34-47.
- Gombash SE, Lee PW, Sawdai E, Lovett-Racke AE. Vitamin D as a risk factor for multiple sclerosis: immunoregulatory or neuroprotective? Frontiers in neurology. 2022;13:796933.
- Taylor SN. Calcium, magnesium, phosphorus, and vitamin D. Nutritional care of preterm infants. 2021;122:122-39.

- De la Guía-Galipienso F, Martínez-Ferran M, Vallecillo N, Lavie CJ, Sanchis-Gomar F, Pareja-Galeano H. Vitamin D and cardiovascular health. Clinical Nutrition. 2021;40(5):2946-57.
- Kumar A, Verma A, Chaurasia RN. Vitamin D and inflammatory cytokines association in mild cognitive impaired subjects. Neuroscience Letters. 2023;795:137044.
- Annweiler C, Beauchet O. Vitamin D-Mentia: Randomized Clinical Trials Should Be the Next Step. Neuroepidemiology. 2011;37(3-4):249-58.
- McCann JC, Ames BN. Is there convincing biological or behavioral evidence linking vitamin D deficiency to brain dysfunction? The FASEB Journal. 2008;22(4):982-1001.
- Eyles DW, Burne TH, McGrath JJ. Vitamin D, effects on brain development, adult brain function and the links between low levels of vitamin D and neuropsychiatric disease. Frontiers in neuroendocrinology. 2013;34(1):47-64.
- 60. Mizwicki MT, Menegaz D, Zhang J, Barrientos-Durán A, Tse S, Cashman JR, et al. Genomic and Nongenomic Signaling Induced by 1α,25(OH) 2-Vitamin D 3 Promotes the Recovery of Amyloid-β Phagocytosis by Alzheimer's Disease Macrophages. Journal of Alzheimer's Disease. 2012;29:51-62.
- Farina N, Llewellyn D, Isaac MGEKN, Tabet N. Vitamin E for Alzheimer's dementia and mild cognitive impairment. Cochrane database of systematic reviews. 2017(1).
- Zhao R, Han X, Zhang H, Liu J, Zhang M, Zhao W, et al. Association of vitamin E intake in diet and supplements with risk of dementia: A meta-analysis. Frontiers in Aging Neuroscience. 2022;14:955878.
- Browne D, McGuinness B, Woodside JV, McKay GJ. Vitamin E and Alzheimer's disease: what do we know so far? Clinical Interventions in Aging. 2019;14(null):1303-17.
- Presse N, Shatenstein B, Kergoat M-J, Ferland G. Low Vitamin K Intakes in Community-Dwelling Elders at an Early Stage of Alzheimer's Disease. Journal of the American Dietetic Association. 2008;108(12):2095-9.
- Denisova NA, Booth SL. Vitamin K and sphingolipid metabolism: evidence to date. Nutrition reviews. 2005;63(4):111-21.
- Emekli-Alturfan E, Alturfan AA. The emerging relationship between vitamin K and neurodegenerative diseases: a review of current evidence. Molecular Biology Reports. 2023;50(1):815-28.