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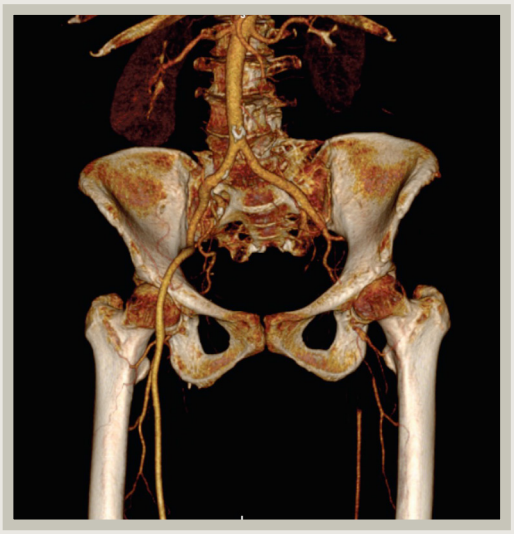

Figure 1. Three dimensional reconstruction of contrast enhanced computed tomography scan demonstrating left external iliac artery thrombosis

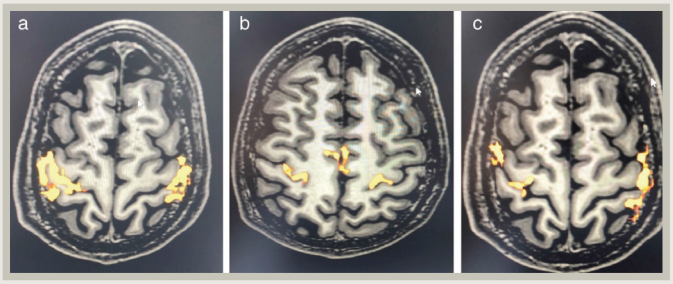

Figure 2. (a-c) In functional magnetic resonance imaging, it was seen that contralateral cortical motor areas were activated when both, hand actively moved and the other hand contracted involuntarily

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About Us

Journal History

Cam ve Sakura Medical Journal (CSMJ) is an international, scientific, open access periodical published journal. It has independent, unbiased, and double-blinded peer-review principles. The journal is the official publication of the Basaksehir Cam & Sakura City Hospital. It is published three times per year (April, August, December). A special supplement including interesting, novel and attractive theme has also been published every year. The publication language of the journal is English.

Title: Cam ve Sakura Medical Journal

Official abbreviation: CSMJ, Csmedj

E-ISSN: 2791-8823

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Aims and Scope

Cam ve Sakura Medical Journal (CSMJ) is an international, scientific, open access periodical published journal. It has independent, unbiased, and double-blinded peer-review principles. The journal is the official publication of the Basaksehir Cam & Sakura City Hospital. It is published three times per year (April, August, December). A special supplement including interesting, novel and attractive theme has also been published every year. The publication language of the journal is English.

Cam & Sakura Medical Journal publishes original experimental or clinical research, review articles, case reports, technical reports, diagnostic puzzle, clinical images, video article, novel insight, and letters to the editor in the field of general medicine. Review articles will be only prepared by expert academicians upon invitation. The journal's target audience includes academics and expert physicians working in all fields of general medicine.

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The editorial and publication process of the journal are shaped in accordance with the guidelines of the International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing.

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Submitted manuscripts are subjected to double-blinded peer-review. The scientific board guiding the selection of the papers to be published in the journal consists of elected specialists of the journal and, if necessary, selected from national and international experts in the relevant field of research. All manuscripts are reviewed by the editor, section associate editors and at least three internal and external expert reviewers. All research articles are interpreted by a statistical editor as well.

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Peer Review, Publication Ethics and Malpractice Statement

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CONSORT statement for randomized controlled trials (Moher D, Schultz KF, Altman D, for the CONSORT Group. The CONSORT statement revised recommendations for improving the quality of reports of parallel-group randomized trials. JAMA 2001; 285:1987-91) (http://www.consort-statement.org/);

PRISMA statement of preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.) (http://www.prisma-statement.org/);

STARD checklist for the reporting of studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al., for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4.) (http://www.stard-statement.org/);

STROBE statement, a checklist of items that should be included in reports of observational studies (http://www.strobe-statement.org/);

MOOSE guidelines for meta-analysis and systemic reviews of observational studies (Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting Meta-analysis of observational Studies in Epidemiology (MOOSE) group. JAMA 2000; 283: 2008-12).

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A list of minimum 4, but no more than 6 keywords must follow the abstract. Keywords in English should be consistent with "Medical Subject Headings (MESH)".

d. Original Article

The instructions in general guidelines should be followed. The main headings of the text should include "Introduction, Material and Methods, Results, Discussion, Study Limitations and Conclusion". The introduction should include the rationale and the background of the study. The results of the study should not be discussed in this part. "Materials and methods" section should be presented in sufficient details to permit the repetition of the work. The statistical methods used should be clearly indicated. Results should also be given in detail to allow the reproduction of the study. The Discussion section should provide a correct and thorough interpretation of the results with the relevant literature. The results should not be repeated in the Discussion Part. The references should be directly related to the findings of the authors. Study Limitation should be detailed in the section. The conclusion section should be highlighted and interpreted with the study's new and important findings.

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Original Articles should be no longer than 3500 words and include no more than 6 tables and 7 or a total of 15 figures and 40 references. The abstract word limit must be 250.

Introduction

The article should begin with a brief introduction stating why the study was undertaken within the context of previous reports.

Materials and Methods

These should be described and referenced in sufficient detail for other investigators to repeat the work. Ethical consent should be included, as stated above.
The name of the ethical committee, approval number should be stated. At the same time, the Ethics Committee Approval Form should be uploaded with the article.

Results

The Results section should briefly present the experimental data in text, tables, and/or figures. Do not compare your observations with that of others in the results section.

Discussion

The Discussion should focus on the interpretation and significance of the findings with concise and objective comments that describe their relation to other work in that area and contain study limitations.

Study Limitations

Limitations of the study should be detailed. In addition, an evaluation of the implications of the obtained findings/results for future research should be outlined.

Conclusion

The conclusion of the study should be highlighted.

e. References

The reference list should be typed on a separate page at the end of the manuscript. Both in-text citations and references must be prepared according to the Vancouver style. Accuracy of reference data is the author's responsibility. While citing publications, preference should be given to the latest, most up-to-date references. The DOI number should be provided for citation of ahead-of-print publication, Journal titles should be abbreviated in accordance with the journal abbreviations in Index Medicus/MEDLINE/PubMed. All authors should be listed in the presence of six or fewer authors. If there are seven or more authors, the first three authors should be listed, followed by "et al." References should be cited in text, tables, and figures should be cited as open source („,4) in parenthesis numbers in parentheses. References should be numbered consecutively according to the order in which they first appear in the text. The reference styles for different types of publications are presented as follows:

i) Standard Journal Article

Salminen P, Paajanen H, Rautio T, et al. Antibiotic therapy vs appendectomy for treatment of uncomplicated acute appendicitis: the APPAC randomized clinical trial. JAMA 2015;313:2340-2348.8.

ii) Book

Getzen TE. Health economics: fundamentals of funds. New York: John Wiley & Sons; 1997.

iii) Chapter of a Book

Volpe JJ: Intracranial hemorrhage; in Volpe JJ (ed): Neurology of the Newborn, ed 5. Philadelphia, Saunders, 2008, pp 481-588.

Porter RJ, Meldrum BS. Antiepileptic drugs. In: Katzung BG, editor. Basic and clinical pharmacology. 6th ed. Norwalk, CN: Appleton and Lange; 1995. p. 361-380.

If more than one editor: editors.

iv) Conference Papers: Bengtsson S, Solheim BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Reinhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sep 6-10;Geneva, Switzerland: North-Holland; 1992. p. 1561-1565.

v) Journal on the Internet: Morse SS. Factors in the emergence of infectious disease. Emerg Infect Dis [serial online] 1995 1(1):[24 screens]. Available from:s URL:http://www/cdc/gov/ncidoc/EID/eid.htm. Accessed December 25, 1999.

vi) Thesis: Kaplan SI. Post-hospital home health care: the elderly access and utilization (thesis). St. Louis (MO): Washington Univ; 1995.

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f. Tables, Graphics, Figures, Pictures, Video:

All tables, graphics or figures should be numbered consecutively according to their place in the text and a brief descriptive caption should be given. Abbreviations used should be explained further in the figure's legend. The text of tables especially should be easily understandable and should not repeat the data of the main text. Illustrations already published are acceptable if supplied by permission of the authors for publication. Figures should be done professionally, and no grey colors should be used. Authors are responsible for obtaining permission to publish any figures or illustrations that are protected by copyright, including figures published elsewhere and pictures taken by professional photographers. The journal cannot publish images downloaded from the Internet without appropriate permission.
Figures or illustrations should be uploaded separately.

Special Sections

Reviews

Reviews will be prepared by authors who have extensive knowledge on a particular field and whose scientific background has been translated into a high volume of publications with a high citation potential are welcomed. These authors and subjects will be invited by the journal. All reviews within the scope of the journal will be taken into consideration by the editors; also, the editors may solicit a review related to the scope of the journal from any specialist and experienced authority in the field.

The entire text should not exceed 25 pages (A4, formatted as specified above).

Reviews should be no longer than 5000 words and include no more than 6 tables and 10 or a total of 20 figures and 80 references. The abstract word limit must be 250.

Case Reports

Case reports should present important and rare clinical experiences. It must provide novel and/or rare clinical data or new insights to the literature. Case reports should consist of an unstructured abstract (maximum 150 words) that summarizes the case. They should consist of the following parts: introduction, case report, discussion. Informed consent or signed releases from the patient or legal representative should be obtained and stated in the manuscript.
Reviews should be no longer than 1000 words and include no more than 200 tables and 10 or a total of 20 figures and 15 references. The abstract word limit must be 150.

Clinical Images

The journal publishes original, interesting, and high quality clinical images having a brief explanation (maximum 500 words excluding references but including figure legends) and of educational significance. It can be signed by no more than 5 authors and can have no more than 5 references and 1 figure or table. Any information that might identify the patient or hospital, including the date, should be removed from the image. An abstract is not required with this type of manuscripts. The main text of clinical images should be structured with the following subheadings: Case, and References.

Video Article

Video articles should include a brief introduction on case, surgery technique or a content of the video material. The main text should not exceed 500 words. References are welcomed and should not be more than 5. Along with the main document, video material and 3 images should be uploaded during submission. Video format must be mp4 and its size should not exceed 100 MB and be up to 10 minutes. Author should select 3 images, as highlights of the video, and provide them with appropriate explanations. Video and images must be cited within main text.

Technical reports

Technical reports are formal reports designed to convey technical information in a clear and easily accessible format. A technical report should describe the process, progress, or results of technical or scientific research or the state of a technical or scientific research problem. It might also include recommendations and conclusions of the research. Technical reports must include the following sections: abstract, introduction, technical report, discussion, conclusions, references. Technical reports should contain less than 20 references.

Diagnostic puzzle

Diagnostic puzzles report unusual cases that make an educational point. Since the aim of these articles is to stimulate the reader to think about the case, the title should be ambiguous and not give away the final diagnosis immediately. Diagnostic puzzles should include an introduction and answer part. The introduction part should include a brief clinical introduction to a case (maximum 250 words) followed by an image and a question designed to stimulate the reader to think about what the image shows. The legend should not indicate the diagnosis but should simply describe the nature of the image. Then, the answer part should appear later (maximum 250 words) outlines a brief description of the key diagnostic features of the image, the outcome, and a teaching point.
Diagnostic puzzles will not include more than 5 references. The quality of the image must be at least 300dpi and in TIFF, JPEG, GIF or EPS format. Videos are also welcome and should be in .mov, .avi, or .mpeg format.

Novel insight

This section will offer an opportunity for articles instead of the traditional category of Case Reports. Submissions to this section should contribute significant new insights into syndromological problems, molecular approach and real novelties on recognized or entirely new genetic syndromes or a new technique. The novel aspect(s) can be in the phenotype and/or genotype, the presentation, and the investigation. Submissions can be based around a single case or serial cases. Manuscripts for this section will go through the usual peer reviewing process. The manuscripts should contain abstract (maximum 150 words), a brief introduction, case report(s) and discussion.

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Instructions to Authors

Letters to the Editor

This section welcomes manuscripts that discuss important parts, overlooked aspects, or lacking parts of a previously published article in this journal. In addition, articles on subjects within the scope of the journal that might have an attraction including educative cases, may also be submitted in the form of a "Letter to the Editor." The manuscripts for this section should be written in an unstructured text including references. The editor may request responses to the letters. There are no separate sections in the text.

Letter to the editors should be no longer than 500 words.

Revision Process

During the submission of the revised version of a manuscript, the authors should submit a detailed "Response to the reviewers and editors" that states point by point how each issue raised by the reviewers and/or editors has been replied to and where it can be found (each reviewer's comment, followed by the author's reply and line numbers where the changes have been made) as well as an annotated copy of the main document. Revised manuscripts should be submitted within 30 days from the date of the decision letter. If the revised version of the manuscript is not submitted within the allocated time, the revision option may be cancelled.

Accepted manuscripts are copy-edited for grammar, punctuation, and format. Once the publication process of a manuscript is completed, it is published online on the journal's webpage as an ahead-of-print publication before it is included in its scheduled issue.

LIMITATION TABLE

Type of Manuscript	Word Limit	Abstract Word Limit	Reference Limit	Table Limit	Figure Limit
Original Article	3500	250 (Structured)	40	6	7 or total of 15 images
Review	5000	250	60	6	10 or total of 20 images
Case Report	1000	150	20	200	10 or total of 20 images
Letter to the Editor	500	No Abstract		No tables	No media
Video Article	500		5		
Diagnostic Puzzle	250 (as a brief clinical introduction		5		
Clinical Images	500 (as a brief explanation)		5	1	1
Technical Reports			20		

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Editorial

Dear Colleagues,

It is a great pleasure for us to publish the first issue of Cam & Sakura Medical Journal (CSMJ) in 2023.

In this issue of CSMJ, you can read the review about long COVID and you will try to find the answer if it is a new syndrome or not. As millions of people all over the world had COVID-19 infection, it will be reasonable to know clinical features of long COVID-19 as a new clinical situation. The brief social anxiety-acceptance and action questionnaire (B-SA-AAQ) has been used to evaluate psychological inflexibility in social anxiety. In this issue, you can read the study which evaluated the reliablity and validity of Turkish adaption of the B-SA-AAQ. You can also access to the study that reported the use of nutritional risk screening-2002 (NRS-2002) tool for evaluation of nutritional risk in patients with COVID-19 pneumonia. Social anxiety disorder is a psychiatric condition in which there is an intense fear of social situations such as social interactions and performing in front of others. Health literacy can be defined as the ability of an individual to obtain and translate knowledge and information in order to maintain and improve health in a way that is appropriate both for the individual and healyth system. Therefore, the individual can obtain, understand, evaluate and apply correct health information for a disability-free life and to be able to maintain quality of life in sickness and in health throughout lifetime. An original article in this issue evaluates the relationship between health literacy and health-seeking behaviors and the characteristics of patients with a chronic disease requiring hospitalization. The last original study in this issue evaluated the association between rhinitis and asthma control. The possible adverse effects of COVID-19 vaccines have been discussed extensively after the global administration of these vaccines during pandemics. In this issue, you can read the case report that defined concomitant peripheral and pulmonary arterial thromboembolism 35 days after COVID-19 mRNA vaccine. Lastly, you can find the case report that reported the use of functional magnetic imaging in congenital mirror movement patient.

I think you will read these articles with great interest. We are waiting your articles and case reports for future issues.

Hoping to meet you on the second issue of 2023.

On Behalf of Deputy Editors, Associate Editors and Editorial Secretary

Merih Çetinkaya

Editor in Chief

Cam & Sakura Medical Journal

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REVIEW

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Long-COVID, is a New Syndrome?

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ABSTRACT

The ongoing or developing new symptoms after acute coronavirus disease-2019 (COVID-19) infection has emerged as a new clinical problem. This has become a problem facing the globally infected population and health systems. "Long-COVID" can be defined as patients with laboratory-confirmed or clinically present COVID-19 whose symptoms persist for four weeks after diagnosis. Symptoms are remarkably heterogeneous, as seen in acute COVID-19. These symptoms may remain stable or fluctuate. Controversy over its definition complicates accurate diagnosis and management of the disease. The most prominent symptoms were fatigue, sleep disturbances, chest pain, and shortness of breath. Recent reports also highlight the risk of long-term sequelae in those recovering from acute COVID-19, affecting almost all organs such as the skin, respiratory system, cardiovascular system, neuropsychiatric system, and renal system. The long-term effects of COVID-19, in hospitalized and non-hospitalized individuals, across all age groups, should be a priority for future research with standardized and controlled studies.

Keywords: Long-COVID, fatigue, COVID-19, sequelae of COVID-19

Introduction

In the Coronavirus disease-2019 (COVID-19) pandemic, some patients with severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection has developed a wide range of physical and mental health problems four or more weeks after acute infection. These symptoms included a wide range of ongoing or newly emerging symptoms that could not be explained by another diagnosis (1,2). Most people with acute infections recover within a few days to a few weeks after infection, so at least four weeks after infection is considered a baseline from which post-COVID conditions can be identified for the first time. Different terminology are used to describe these long-lasting symptoms, including "long-COVID", "post-COVID syndrome", "postacute COVID-19", "chronic COVID-19", "post-COVID conditions", and "postacute sequelae of SARS-CoV-2 infection". Whether this set of symptoms represents a new syndrome specific to COVID-19 has yet to be determined (3,4).

Symptoms seen after COVID-19 can occur in different ways (3);

- Persistent symptoms that begin at the time of acute COVID-19 illness,

- New -onset symptoms following an asymptomatic illness or the remission period of acute illness,

- The addition of new symptoms or clinical conditions (e.g., cognitive difficulties) over time, in addition to some persistent symptoms associated with an already existing disease (e.g., shortness of breath),

- Worsening of pre-existing symptoms or conditions.

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Symptoms

These long-lasting symptoms can occur following both mild and severe acute COVID-19 illness. These symptoms can be categorized under two different headings: physical and psychological symptoms (3,5,6,7,8,9,10).

Physical symptoms can be seen in one-third or more of the patients. Commonly reported physical symptoms include:

- Fatigue
- Cough
- Dyspnea
- Chest pain

Less common are anosmia, arthralgia, headache, rhinitis, dysgeusia, anorexia, dizziness, myalgia, insomnia, alopecia, sweating, decreased libido, and diarrhea.

Psychological and cognitive complaints may occur more frequently than in those recovering from other similar illnesses (8,10,11). It has been reported to be especially common among patients followed up in the intensive care unit (8). The main disorders seen are worsening quality of life, anxiety/depression, and persistent psychological symptoms (5,6,9). In one study, memory impairment was reported in 21% of patients with mild illness and no hospitalization (11).

At least one component of post-intensive care syndrome has been reported in at least three-quarters of COVID-19 survivors (10,12). The most common symptoms of this syndrome are physical weakness (39%), joint stiffness/pain (26%), mental/cognitive dysfunction (26%) and myalgias (21%) (10). Other psychological or cognitive complaints likely to occur are post-traumatic stress disorder, anxiety, depression, and poor memory and concentration.

Symptoms related to post-COVID conditions are summarized below (1,3);

General symptoms

- Fever
- Disturbing fatigue
- Symptoms worsened by physical or mental effort

Respiratory and heart symptoms

- Cough
- Difficulty breathing
- Chest pain
- Heart palpitations

Neurological symptoms

- Headache
- Sleep difficulties
- Difficulty in thinking or concentrating (brain fog)
- Dizziness when standing up
- Depression or anxiety
- Changes in smell or taste

Digestive symptoms

- Diarrhea

Other symptoms

- Arthralgiaand myalgia
- Changes in menstrual cycles
- Rash

Among children, although data are limited, the prevalence of persistent symptoms appears lower (1,13). The most commonly reported symptoms were fatigue (3%) and impaired concentration (2%).

The reason why there are such heterogeneous post-COVID conditions may be due to different underlying pathophysiological processes, such as (3);

- Organ damage due to acute phase disease
- Complications from uncontrolled inflammation
- Ongoing viral activity due to a possible in-host viral reservoir
- Inadequate antibody response
- Autoimmunity

Course of Recovery

While most patients with mild acute COVID-19 illness are expected to recover quickly (e.g. two weeks), those with moderate to severe illness may take two to three months, sometimes longer. Another reason for this difference in recovery time may be the underlying premorbid risk factors (14). A longer recovery period is expected in elderly patients with comorbidities, in patients who develop complications during acute illness (e.g. secondary bacterial pneumonia, venous thromboembolism, multisystem inflammatory syndrome) and in patients with prolonged hospitalization or needed intensive care and people who did not obtain COVID-19 vaccine (1,5,8,10,15). It seems that the best way to prevent long COVID-19 in the current situation is not to obtain the disease (1,2).

General Evaluation

There are several guidelines for COVID-19 follow-up after acute illness developed by several organizations

(3,4,16,17,18,19,20). The severity of the previous illness should be taken into account when deciding whether to follow-up the patient. Patients with mild-to-moderate illness that has not required hospitalization do not need to routinely schedule a COVID-19 follow-up visit unless the patient requests one or has progressive or new symptoms. Patients with more severe acute COVID-19 disease who had been hospitalized would be offered a follow-up examination within 2 to 3 weeks at the latest (2). When the patient presents for a follow-up examination, a comprehensive history of COVID-19 should be taken, including the length of hospitalization, complications, treatments given, etc. Physical examination must be performed in detail in patients who have had COVID-19 (3,4,21).

Patients presenting with persistent or increasing respiratory symptoms, fatigue, or weakness should undergo detailed assessment, such as ambulatory pulse-oximetry, in addition to standard vital signs (e.g. blood pressure, heart rate, respiratory rate, pulse-oximetry, body temperature). Orthostatic vital signs may be important for individuals reporting postural symptoms, dizziness, fatigue, cognitive impairment, or weakness (4,21).

The laboratory tests must be ordered on the basis of abnormal tests during the illness and the present symptoms. For most patients recovering from mild acute COVID-19, laboratory testing is not necessary. For patients with ongoing symptoms, it is reasonable to do the basic panel of laboratory tests (2,4,21):

- Complete blood count
- Blood chemistry, including electrolytes and renal function
- Liver function studies, including serum albumin
- Inflammatory markers, C-reactive protein, erythrocyte sedimentation rate, and ferritin

For selected patients:

- Brain natriuretic peptide and troponin, (in patients with heart failure or complicated by myocarditis or with possible cardiac symptoms such as dyspnea, chest discomfort, edema)
- D-dimer (in patients with unexplained persistent or new dyspnea or in any patient with suspected of thromboembolic disease)
- Thyroid function tests in patients with unexplained and persistent fatigue or malaise
- Creatinine kinase in patients with weakness or muscle tenderness
- Antinuclear antibody, rheumatoid factor, anti-cardiolipin, etc. for rheumatological conditions

COVID-19 testing and serology does not need to be routinely retested to establish a diagnosis of post COVID conditions. Serologic testing may be performed for recovering plasma donation or for evaluation of unexplained symptoms in patients with no prior positive COVID-19 serology (2,21).

Management

The primary goal of medical management in these patients is to optimize the quality of life. And these patients should be consulted or referred to relevant specialists for a comprehensive management plan based on their current symptoms and underlying physical and psychiatric conditions (4).

For example; for the following cardiopulmonary problems, the patient would be referred to cardiology or pulmonology if necessary. Ongoing dyspnea, cough, chest discomfort, pleuritic pain, wheezing, orthopnea, chest pain, peripheral edema, palpitations, dizziness, orthostasis, and pre-syncope or syncope are questioned in detail. A comprehensive cardiopulmonary evaluation should be performed based on the basis of their clinical history and findings. Follow-up chest imaging, typically chest radiography at 12 weeks, is recommended for all patients in whom a pulmonary infiltrate or other abnormality is detected on imaging during the acute course of COVID-19. Imaging should be performed without delay, particularly in patients with new or progressive respiratory symptoms. Chest computed tomography (CT) may be preferred if malignancy is suspected, or high-resolution CT may be an appropriate imaging study for patients with suspected interstitial lung disease such as acute respiratory distress syndrome (ARDS). Pulmonary function tests may be a good choice in patients with persistent, progressive, or emerging respiratory symptoms and in patients recovering from ARDS (22,23).

Referral to neurology and psychiatry departments for ongoing or progressive or new neurologic or neurocognitive problems is appropriate. Neurological imaging is typically not recommended unless there is concern for an unexplained neurological deficit or focal lesion or other conditions (4).

It is recommended that all patients be evaluated for signs and symptoms of deep venous thrombosis, pulmonary embolism, or arterial thrombosis (e.g. digital ischemia) in the upper and lower extremities. Patients with documented thromboses are treated similarly to thromboses in non-COVID-19 patients (2).

In addition to these symptoms, note that invasive fungal infections such as rhino-orbital mucormycosis, have been reported in patients recovering from COVID-19. As known, treatment with corticosteroids and poorly controlled diabetes mellitus are the main risk factors for mucormycosis (24,25). In acute COVID-19 patients with these risk factors, mucormycosis should be suspected if sinus congestion, blackish or colorless nasal discharge, facial or eye pain, or visual symptoms are detected following the acute period (26). Other infectious complications have also been observed in COVID-19 patients with these risk factors, including pulmonary aspergillosis (27) and strongyloides hyperinfection (28). Although these infectious complications are generally considered a late complication of acute illness, note that they can also occur late in patients recovering from moderate to severe COVID-19.

Patients with persistent taste and/or olfactory disturbances may benefit from further evaluation and management, and should be bereferred to an otolaryngologist (2). Adequate rest, good sleep hygiene, and specific fatigue management strategies may be recommended for patients with persistent fatigue (2).

Additionally, it is good and necessary to be transparent with the patient for the process of goal setting and make it clear that post COVID conditions are not yet well understood, so well as the type, duration, severity, and recovery of post COVID conditions differ among patients.

It would not be wrong to say that the challenging pandemic period we have experienced in the last two years has given us doctors a lot to learn professionally, but considering current knowledge, we can easily say that we still have a long way to go.

Ethics

Peer-review: Externally and internally peer-reviewed.

Financial Disclosure: The author declared that this study received no financial support.

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Reliability and Validity Study of the Turkish Version of the Brief Social Anxiety-Acceptance and Action Questionnaire

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What is known on this subject?

The Brief Social Anxiety-Acceptance and Action Questionnaire (B-SA-AAQ) can measure psychological inflexibility in context of social anxiety.

What this study adds?

Turkish version of the B-SA-AAQ.

ABSTRACT

Objective: Experiential avoidance is closely related to social anxiety, which is a condition characterized by intense fear in social situations, including social interactions and performing in front of others.

Material and Methods: The sample of this study consisted of 113 people. The data were obtained using a demographic form, Brief Social Anxiety-Acceptance and Action Questionnaire (B-SA-AAQ), Acceptance and Action Questionnaire-II (AAQ-II), and hospital anxiety and depression scale (HADS). Internal consistency and item-total correlation were evaluated with Cronbach's alpha coefficient. Confirmatory factor analysis (CFA) was used to test the factor structure. Temporal stability was assessed using the test-retest method.

Results: The Turkish adaptation of the B-SA-AAQ was found to have good internal consistency with a Cronbach's α coefficient of 0.899. CFA indicated a two-factor structure with acceptable fit indices [χ^2: 22.8, degrees of freedom: 13; root mean square error of approximation (RMSEA): 0.0817; RMSEA 90% confidence interval (CI) lower bond: 0.013, RMSEA 90% CI upper bond: 0.136, CFI: 0.978; Tucker-Lewis index: 0.965)]. The B-SA-AAQ and its subscales were significantly correlated with the AAQ-II and HADS ($p<0.05$). The results of the test-retest correlation analysis indicated temporal stability.

Conclusion: Therefore, the B-SA-AAQ is a reliable and valid scale for measuring experiential avoidance and psychological flexibility in the context of social anxiety.

Keywords: Acceptance and commitment therapy, social phobia, anxiety, depression

Introduction

Social anxiety disorder (SAD) is a prevalent psychiatric condition that affects individuals globally. The defining feature of SAD is an intense fear of social situations, including social interactions and performing in front of others. Individuals with SAD often experience significant distress when subjected to negative evaluations from others and may cope by avoiding social interactions. Worldwide, lifetime prevalence has been reported between 0.2% and 12.1%. People with SAD rarely get better on their own. Symptoms tend to be persistent and chronic. Additionally, it is often associated with an increased risk

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of secondary depression, other anxiety disorders, mood disorders, and impulse control disorders (1,2).

SAD is related to experiential avoidance (3,4). Experiential avoidance refers to a behavioral pattern in which an individual avoids contact specific undesired experiences, including fear-related sensations, thoughts, feelings, memories, and urges to take certain actions. This avoidance behavior is aimed at escaping or evading these psychological events and the situations that trigger them (5). Attempting to escape or avoid a social situation for not experiencing humiliation, social fear, physiological discomfort, and emotional distress may be stated as experiential avoidance related to social phobia. Generalized experiential avoidance may lead to repertoire narrowing (6). Avoidance may act as a barrier to experiencing meaningful social interactions (4). Psychological inflexibility can be defined as the inflexible and rigid prioritization of psychological reactions over chosen values and contingencies when guiding one's actions. This often manifests when individuals try evading or avoid unwanted internal experiences such as thoughts and emotions (7). To put it simply, psychological inflexibility refers to a pattern where an individual's thoughts exert excessive control over their behavior, feelings, and other internal experiences. Alternatively, they may choose to avoid these experiences at the cost of more effective and meaningful actions. These behaviors are believed to play a role in the development, continuation, and worsening of various psychological issues. Both psychological inflexibility and experiential avoidance are thought to contribute to a wide range of mental health problems (8). Numerous studies have been conducted to evaluate the effectiveness of acceptance and commitment therapy, which is rooted in the principles of psychological flexibility, on social anxiety (SA) (9).

Hayes (5) first created the acceptance and action form (AAQ) to assess psychological flexibility/inflexibility. Although it has been widely used for a while, due to low internal consistency, difficulty to understand, and unstable factor structure, a shorter acceptance and action form-II (AAQ-II) was developed (10). This scale is one of the most frequently used scales to evaluate psychological flexibility/inflexibility, which the participant himself filled in.

Experiential avoidance studies show the need for new measures-so AAQ forms for specific contexts or problems (11,12,13). One of them is Social Anxiety-Acceptance and Action Questionnaire (SA-AAQ) (14). Later, MacKenzie et al. (15) developed the short form of SA-AAQ (brief SA-AAQ), aiming to create a scale that can be filled in a shorter time and more easily applied. Using the SA-AAQ as a foundation, researchers constructed an eight-item, two-factor (acceptance and action) model that included. This model has favorable levels of reliability, as well as convergent, discriminant, and incremental validity. The model also showed a strong positive correlation with the 19-item SA-AAQ in both clinical and non-clinical populations. Cronbach's alpha values of the entire scale, acceptance, and action factors were 0.81, 0.84, and 0.72, respectively (15).

A scale to evaluate the psychological flexibility model, which plays a role in developing and treating anxiety disorders, will provide an essential tool for clinicians and researchers working with SA. Therefore, this study examined the psychometric properties and factor structure of the Turkish adaption of the brief Social Anxiety-Acceptance and Action Questionnaire (B-SA-AAQ) in non-clinical samples. The primary aim of the study was to assess the validity and reliability of the B-SA-AAQ in a Turkish-speaking non-clinical population. Specifically, the study confirms the two-factor structure of the original scale and establish its effectiveness as a tool for measuring experiential avoidance related to SA. A second hypothesis is that experiential avoidance measured by B-SA-AAQ is related to experiential avoidance in general, depression, and anxiety.

Material and Methods

Participants

The individuals, aged 18-65, accepted to participate in the research voluntarily included in this research. The sample consisted of 122 individuals who work in research and training hospital. Nine of 122 participants were identified as outliers by the box plot method, and the data analyzed in the study were collected from 113 individuals.

Procedure

The study was approved by the Ethics Committee of Alaattin Keykubat University (decision no: 11-01, date: 02.11.2022). Before conducting the study, permission was obtained from the developers of the original B-SA-AAQ questionnaire. The Turkish translation of the scale was developed by translating the items into Turkish and then back to English by two bilingual psychiatrists to ensure its accuracy. The Turkish B-SA-AAQ and socio-demographic forms were then administered to the participants. The AAQ-II and hospital anxiety and depression scale (HADS) were also used as measures of psychopathology to investigate the validity of the scale.

Measurement Tools

Demographic Form: The form was developed by researchers and includes questions about age, gender, education, and psychiatric history.

B-SA-AAQ: It was developed to assess the psychological flexibility associated with social phobia by MacKenzie et al. (15). The 7-point Likert-type scale consists of 8 items. The original scale was confirmed using a clinical and a non-clinical sample. Results indicated that an eight-item, two-factor model (acceptance and action) provided a good fit for the B-SA-AAQ in both samples (15).

AAQ-II: It was developed by Bond et al (10). The validity and reliability analyses of the AAQ's new version, which consists of seven items, provided strong statistical evidence across both clinical and non-clinical samples. Furthermore, elevated scores on the scale were found to be indicative of increased levels of psychological inflexibility, leading to a rise in experiential avoidance. The Turkish adaption study of AAQ-II was conducted by Yavuz et al. (16).

HADS: Zigmond and Snaith (17) developed a scale comprising 14 items, of which seven are aimed at assessing anxiety symptoms, and the remaining seven measure depression symptoms. Participants rate the items on a 4-point Likert scale, and scores can range from 0 to 3. The Turkish adaptation of HADS was conducted by Aydemir (18).

Statistical Analysis

For descriptive statistics and psychometric analysis, we used Jamovi version 2.3.21.0. The data underwent tests for univariate and multivariate normality, linearity, and homogeneity of sample variances. Outliers were also checked for. Cronbach's alpha and Pearson's correlation coefficients were used to evaluate internal consistency and item-total correlation. The temporal stability of the Turkish B-SA-AAQ was evaluated by the test-retest correlation, which involved a follow-up assessment a week after the baseline assessment, and then evaluated the results using Pearson's correlation test. To test the two-factor structure obtained from the original form, confirmatory factor analysis (CFA) was used. Their goodness of fit to data can also evaluate the quality of models. Chi-square (χ^2) is very sensitive to sample size; for this reason, relative chi-square was used, which is the chi-square fit index divided by degrees of freedom (χ^2/df), making χ^2 less dependent on sample size. Additionally, also the comparative fit index (CFI), the Tucker-Lewis index (TLI), and the root mean square error of approximation (RMSEA) were used to evaluate the goodness of fit.

Results

Descriptive Statistics

Analyses were conducted with data from 113 people. Seventy-nine were females (69.9%). The mean age was 29.1 (standard deviation: 6.11, range between 18 and 58) (Table 1).

Reliability Analysis

The Cronbach's alpha coefficient was calculated as 0.825 for the internal consistency of the B-SA-AAQ scale with the initial eight items. In the item-total score analysis, the lowest correlation was -0.15 for the 7th (B-SA-AAQ-7) item (Table 2). When the 7th item was deleted, Cronbach's alpha coefficient increased significantly (0.825 to 0.899), and the correlation of this item was significantly lower than other items. For this reason, item 7 has been removed from the scale for ongoing analysis.

For the temporal reliability analysis, 12 participants from the sample refilled B-SA-AAQ one week later the test-retest analysis. Correlation coefficients were calculated by Spearman correlation analysis between 0.824-0.858 for B-SA-AAQ and subscales, and all values were statistically significant ($p<0.001$). The Cronbach's alpha coefficient was calculated as 0.899 for the internal consistency of the B-SA-AAQ Action subscale 0.774 and 0.865 for the SA-AAQ acceptance subscale.

Construct Validity

CFA was conducted to validate the construct of B-SA-AAQ in Turkish. The CFA of the 7-item structure of B-SA-AAQ was validated and found to have the same two-factor structure as the original B-SA-AAQ in English. Fit indices from the analysis showed good to excellent (χ^2: 22.8, df: 13; RMSEA: 0.0817; RMSEA 90% CI lower bond: 0.013, RMSEA 90% CI upper bond: 0.136, CFI: 0.978; TLI: 0.965). Additionally, all factor loading values are significant ($p<0.001$) (Table 3).

Criterion Validity

The relationships between B-SA-AAQ, AAQ-II, and HADS with B-SA-AAQ were evaluated by pearson correlation analysis for criterion-related validity (Table 4).

Table 1. Socio-demographic variables

Age mean, SD		29.1	6.11
Sex (n, %)	Women	79	69.9
	Men	34	30.1
Education level (n, %)	High school	4	3.6
	University	57	50.4
	Postgraduate	52	46.0
History of psychiatric disorder (n, %)	Yes	33	70.8
	No	80	29.2

n=113, SD: Standard deviation

Discussion

This study aimed to assess the reliability and validity of the Turkish version of B-SA-AAQ, which measures experiential avoidance in SA based on the SA-AAQ. A sample size of at least 5-10 participants per variable was recommended for the analysis of the scale's construct validity. The sample size for this study was 113 individuals who met this criterion. One of the study's hypotheses was that the Turkish version of B-SA-AAQ would preserve the two-factor structure of the original version. CFA was conducted to test this hypothesis, and it showed that B-SA-AAQ has a two-factor structure, with acceptable goodness-of-fit values.

Table 2. Item-total statistics, Cronbach's alpha if item deleted for initial eight items

Item	Cronbach's alpha if item deleted	Corrected item-total correlation
B-SA-AAQ-1	0.785	0.693
B-SA-AAQ-2	0.770	0.776
B-SA-AAQ-3	0.766	0.826
B-SA-AAQ-4	0.791	0.640
B-SA-AAQ-5	0.802	0.572
B-SA-AAQ-6	0.807	0.537
B-SA-AAQ-7	0.899	-0.150
B-SA-AAQ-8	0.780	0.730

B-SA-AAQ: Brief Acceptance and Action Questionnaire for Social Anxiety

The first, third, and fifth items constitute the action subscale, and the second, fourth, sixth, and eighth items constitute the acceptance subscale. The Cronbach's Alpha coefficient was 0.82 for the action subscale, 0.87 for the acceptance subscale, and 0.90 for the total score on the original scale. The study's results indicated adequate internal consistency of the Turkish version of B-SA-AAQ and its subscales. Furthermore, the temporal stability of the scale was assessed through a test-retest reliability analysis conducted one week after the baseline assessment. In test-retest analysis, two scores of B-SA-AAQ at two different times have a strong correlation for all items ($p<0.001$). This result indicates the temporal stability of B-SA-AAQ and the subscales of B-SA-AAQ.

Pearson's correlation coefficients were used to evaluate the relationships between the action and acceptance subscales, total scores of B-SA-AAQ and the AAQ-II. Given that both scales measure psychological inflexibility and experiential avoidance, it was expected that there would be moderate-to-strong correlations. The results revealed significant correlations ($p<0.001$) between the total and subscale scores of B-SA-AAQ and AAQ-II, supporting the hypothesis that B-SA-AAQ can measure psychological inflexibility by assessing experiential avoidance. This result provides evidence of convergent validity, and previous studies had similar results (14,15). B-SA-AAQ may have two advantages over AAQ-II. The first is that it makes a context-specific assessment of SA. Tools for measuring experiential avoidance in a specific context can be more sensitive than generic ones such as AAQ-II. The second advantage is that it has a two-factor structure:

Table 3. Model-fit results of confirmatory factor analysis for Turkish B-SA-AAQ

Factor	Item	Estimate	SE	Z	p
Action	B-SA-AAQ-1	1.186	0.138	8.60	<0.001
	B-SA-AAQ-3	0.987	0.144	6.86	<0.001
	B-SA-AAQ-5	1.542	0.144	10.71	<0.001
Acceptance	B-SA-AAQ-2	1.289	0.146	8.84	<0.001
	B-SA-AAQ-4	1.680	0.154	10.93	<0.001
	B-SA-AAQ-6	1.655	0.133	12.40	<0.001
	B-SA-AAQ-8	1.423	0.180	7.92	<0.001

B-SA-AAQ: Brief Acceptance and Action Questionnaire for Social Anxiety, SE: Standard error

Table 4. Pearson Correlation coefficients for criterion-related validity analysis

	B-SA-AAQ-action	B-SA-AAQ-acceptance	B-SA-AAQ -total
AAQ-II	0.520**	0.465**	0.516**
HADS-anxiety	0.315**	0.203*	0.262*
HADS-depression	0.308**	0.255*	0.293*

**p<0.05, **p<0.01. AAQ-II: Acceptance and action questionnaire-II, HADS: Hospital anxiety and depression scale, B-SA-AAQ: Brief Acceptance and Action Questionnaire for Social Anxiety*

acceptance and action. Acceptance refers to the willingness to experience unwanted internal events, and action refers to acting consistently with values.

Psychological inflexibility and experiential avoidance in general and in people with social phobia are correlated with depression and anxiety as hypotheses (15,16). The correlations of HADS, total scores, and subscales of B-SA-AAQ evidenced the convergent validity of B-SA-AAQ. The action subscale of B-SA-AAQ correlates moderately with anxiety and depression subscales of HADS ($r=0.315$, $r=0.308$, $p<0.001$). Additionally, the acceptance subscale ($r=0.203$, $r=0.255$, $p<0.05$) and total scores ($r=0.262$, $r=0.293$, $p<0.05$) of B-SA-AAQ correlate small with the anxiety and depression subscales of HADS. According to these results, despite B-SA-AAQ being developed to assess experiential avoidance related to SA, it can also be a valuable tool for predicting depression and anxiety in general in the context of SA.

The lack of psychological flexibility is considered a critical factor in SAD and leads to the disorder's continuation or persistence and intensification (19). There is a need for easily applicable tools for the rapid assessment of SA and related psychological processes. The abbreviation of the original scale and its translation into Turkish can be helpful in this respect. SA-AAQ has been translated into Korean, Persian, Portuguese, and Thai. However, there is no reliability and validity study for B-SA-AAQ other than the original language. Thus, this may be one of the first versions of B-SA-AAQ other than the original language.

Study Limitations

This study has some limitations that need to be taken into consideration. First, the sample used in the study was non-clinical. Therefore, the results of this study may not be generalized to clinical populations. The primary aim of the study was to provide a Turkish adaptation of the B-SA-AAQ, which offers preliminary evidence for its validity and reliability in the Turkish language. Second, the severity of SA symptoms in the participants was not assessed. Third, due to the cross-sectional design of the study, causal relationships cannot be determined. Future longitudinal studies are needed to explore causal relationships.

Overall, the results of the current result indicated that the B-SA-AAQ is a reliable and valid scale that can measure experiential avoidance. B-SA-AAQ can be an alternative to the AAQ-II and other psychological inflexibility scales for measuring experiential avoidance and psychological inflexibility in people with SA. Furthermore, this scale can be used to tract changes in interventions for managing SA.

Conclusion

In conclusion, the result of the current study stated that the form for the Turkish adaption of the B-SA-AAQ has acceptable reliability and validity, despite some limitations. This measurement tool can examine studies on psychological inflexibility, which has a place in developing and maintaining SA in the national literature and clinical practices. Including this scale in the existing collection of context-specific versions of the AAQ in Turkish can make a valuable contribution to the research on psychological inflexibility and experiential avoidance. Therefore, it may be recommended to support the scale's psychometric properties with samples with different characteristics in the future.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of Alaattin Keykubat University (decision no: 11-01, date: 02.11.2022).

Informed Consent: Participants were instructed on the purpose and design of the study, and informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.B.A., H.Ş.B., T.K., Concept: F.B.A., Design: F.B.A., H.Ş.B., Data Collection or Processing: H.Ş.B., Analysis or Interpretation: F.B.A., H.Ş.B., Literature Search: F.B.A., T.K., Writing: F.B.A., H.Ş.B., T.K.

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Impact of Nutritional Status on Prognosis in Non-critically ill Patients with COVID-19 Pneumonia

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What is known on this subject?

The current studies have shown that malnourished patients had higher treatment costs and worse prognosis and a longer duration of the hospitalization. Several tools such as nutritional risk screening-2002 (NRS-2002), malnutrition universal screening tool, and mini nutritional assessment-short form (MNA-SF) have been developed and used to assess the nutritional status in hospitalized patients. The NRS-2002, MNA-SF, and the nutritional risk index have been reported to be useful and practical for the NRS-2002 in the coronavirus disease-2019 (COVID-19). The NRS-2002 was found to be more effective than body mass index in predict the prognosis of the COVID-19, especially in elderly patients.

What this study adds?

We suggest that a simple, user-friendly NRS-2002 tool should be performed to evaluate the nutritional risk in COVID-19 pneumonia in routine clinical assessments. Performing NRS-2002 more than once in the hospitalization process may help the physicians in the early treatment of malnutrition and improve the prognosis of the disease.

ABSTRACT

Objective: The study assessed the nutritional status of non-critically ill coronavirus disease-2019 (COVID-19) patients with pneumonia using the nutritional risk screening 2002 (NRS-2002) score and evaluate ıts impact on prognosis.

Material and Methods: The clinical presentation of COVID-19 disease varies widely from asymptomatic or mild upper respiratory infection to severe life-threatening pneumonia and respiratory failure. Malnutrition negatively affects impair prognosis in COVID-19 patients, but few studies have evaluated the prognostic value of nutritional risk in COVID-19. In this retrospective observational study, non-critically ill COVID-19 patients who were divided into two groups considering their nutritional risk (NRS-2002 score < or ≥3) were compared to each other. Data analysis was performed using SPSS version 22 (Chicago, IL, USA).

Results: A total of 142 non-critically ill patients with COVID-19 were included in the study. The patients with the nutritional risk (NRS-2002 score ≥3) were older and had higher mortality and intensive care unit (ICU) requirement rates than those without the nutritional risk. The groups did not differ regarding gender distribution, body mass index, and length of hospital stay. Compared with survivors, patients who died (n=11, 7.75%) were older and had significantly higher NRS-2002 scores and C-reactive protein levels and lower oxygen saturation and albumin level.

Conclusion: The NRS-2002 test is a practical tool that can help assess the need for ICU admission and mortality in patients with COVID-19 pneumonia. The application of the test early during the disease should be considered for risk assessment, particularly in elderly patients.

Keywords: SARS-CoV, pneumonia, malnutrition, prognosis

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Introduction

Coronavirus disease-2019 (COVID-19) disease is caused by a newly identified type of coronavirus called severe acute respiratory syndrome-coronavirus-2. The virus was first discovered in December 2019, in China and led to a global pandemic that presents with a broad spectrum of clinical manifestations ranging from asymptomatic or mild upper respiratory infection to severe life-threatening pneumonia and respiratory failure. Like almost every viral disease, fever due to acute inflammatory process, anorexia, and subsequent weight loss are common in COVID-19 disease (1).

The first COVID-19 case in Turkey was reported on March 11, 2020 (2). Since then, as in other countries in the world, the number of infected people has increased rapidly. The mortality of the COVID-19 infection was found especially high in elderly patients. Comorbidities such as hypertension, diabetes mellitus (DM), chronic obstructive pulmonary disease, malnutrition, and cancer have been reported as risk factors for the progression of the COVID-19 in the previous studies (3). These studies reported a higher prevalence of DM and malnutrition in older patients with the COVID-19 than in the general population. The results of the studies conducted in Italy and the USA were in contrast with observations from China and those studies pointed out that the severity of COVID-19 was closely related to obesity (4,5). The diagnosis and treatment of malnutrition are crucial for a better prognosis of the COVID-19 disease (6). Malnutrition is a clinic phenomenon that is mostly underdiagnosed and defined simply as imbalanced feeding, under or overfeeding, and affects both thin and obese people (7).

The current studies have shown that malnourished patients had higher treatment costs and worse prognosis and a longer duration of the hospitalization (3). Several tools such as nutritional risk screening (NRS-2002), malnutrition universal screening tool (MUST), and mini nutritional assessment-short form (MNA-SF) have been developed and used to assess the nutritional status in hospitalized patients (3,8). The NRS-2002, MNA-SF, and the nutritional risk index have been reported to be useful and practical for the NRS-2002 in the COVID-19 disease (9). The NRS-2002 was found to be more effective than BMI in predict the prognosis of the COVID-19, especially in older patients (10). To our knowledge, the prognostic value of the nutritional risk in the COVID-19 (disease) was evaluated specifically in several studies, but there is a need for more studies besides the current studies (11). We assess the nutritional status of non-critically ill COVID-19 patients with pneumonia using the NRS-2002 test and evaluate its impact on the prognosis of the disease.

Material and Methods

Subjects

Patients admitted to the hospital and treated with a diagnosis of COVID-19 pneumonia between March 2020 and June 2020 were included in our study. The records of the patients consisting of demographic features, co-morbidities, and laboratory findings were noted. The diagnosis of COVID-19 was reached by polymerase chain reaction (PCR) testing of the oronasal swab for the presence of reminiscent lesions as predominantly peripheral ground-glass opacities at lower lung zones suggesting COVID-19 on chest computed tomography, history of contact with an infected patient, or fever (>37.3°C), cough, sputum, or presence of gastrointestinal symptoms, lymphopenia, and ruling out other causes led us to a diagnosis of COVID-19 PCR negative.

The patients and the criteria for hospitalization, infection severity, admission to an intensive care unit (ICU), and discharge were managed according to the Turkish Ministry of Health's COVID-19 management guidelines (2). According to the rules of the Turkish Ministry of Health, evaluation and recording of the nutritional status of all in-patients by the nursing staff using NRS-2002 is mandatory. The first part of NRS-2002 was filled by in-service nurses within the first 24 h of admission; if NRS-2002 score ≥3, the second part is filled by the physicians.

The NRS-2002 were evaluated by asking the following 4 questions:

- Is the body mass index (BMI) <20.5 kg/m^2?

- Has the patient lost weight within the last week?

- Has the patient had a reduced dietary intake during the last week?

- Is the patient severely ill?

A patient was "not at risk" if BMI is ≥20.5 kg/m^2, food intake was normal, the weight has not been declining and the current illness was not severe (i.e., no increased stress metabolism). If at least one of these criteria was met, and the assessment results in by giving a score from 0-3 concerning BMI, recent weight loss, and food intake during the previous weeks. Furthermore, stress metabolism was evaluated with a 0-3 score according to the illness category. Finally, the patients aged 70 years and older get one extra point. Patients with an NRS-2002 score ≥3 were accepted as risky nutritionally according to the European Society of Clinical Nutrition and Metabolism (ESPEN) (7). BMI was classified into the following categories: underweight (<18.5 kg/m^2), healthy weight (18.5-24.9 kg/m^2, overweight (25-29.9 kg/m^2), and

obesity ≥30 kg/m^2). Therefore, according to the presence or absence of nutritional risk, our patients were separated into two groups. The demographic features, comorbidity, laboratory findings, length of stay (LOS), and mortality rate in the hospitalization, the requirement of ICU was compared between the two groups. Those under 18 years of age and pregnant were excluded from the study. This study was approved by the University of Health Sciences Turkey, Istanbul Training and Research Hospital Ethical Committee (12.06.2020-2400). The study was performed appropriate to the rules in the Helsinki Declaration.

Statistical Analysis

Continuous variables were presented as mean ± standard deviation or median (range) and categorical data as percentages as appropriate. Differences between the groups were assessed using a Student's t-test. Categorical data were compared using the X^2 test: a p value of <0.05 was accepted as significant. The risk factors for mortality were evaluated with cox regression analysis. Results are presented as an odds ratio (OR) with confidence intervals (CI) of 95%. Data analysis was performed using SPSS version 22(SPSS Inc., Chicago, IL, USA).

Results

A total of 142 COVID-19 patients 82 (57.7%) males and 60 (42.2%) females and the median age was 55 and interquantil range was (42.7-66.2). The minimum age was 21 years, and the maximum was 94 years. The most common associated condition was DM with 31 cases (21.8%). Eleven cases (7.7%) die, and 13 cases (9.2%) required ICU admission. In 59 (41.5%) cases, the PCR test was positive.

The BMI of patients was classified according to the World Health Organization. In the current study, underweight, normal, overweight, and obese were found in 1.4%, 38.4%, 37.3%, and 23.2% of cases, respectively.

According to NRS-2002, 11 patients (7.7%) had an NRS-2002 score of 3 and over, and were considered as nutritionally at-risk. NRS-2002 score 0:60 (42.3%), score 1:37 (26.1%), score 2:34 (23.9%), score 3:7 (4.9%), score 4:3 (2.1%), and score 6:1 (0.7%).

They were elder and had higher mortality rates, and higher ICU requirement rate than cases with a nutritional risk score of <3. Four of eleven cases had normal BMI, but the rest of the group were overweight and obese. There was not any statistically significang difference between the albumin levels, BMI, BMI class, length of hospital stays, and gender distribution of these 2 groups (Table 1). The NRS-2002 score of 3 or more was higher in patients aged over 65 than under 65 (17.5% vs. 3.9%, respectively). In other words, the malnutrition risk in the aged ≥65 age group was 5 times more than in patients under 65 years of age (OR: 5.1 , 95% CI: 1.43-18.8 ; p value=0.006).

Eleven (7.75%) cases died. Deceased patients were elderly, had significantly higher NRS-2002 scores, and C-reactive protein (CRP), also had lower oxygen saturation and albumin levels than the patients who survived. Gender, BMI, and weight distribution were not different between the groups (Table 2).

The NRS-2002 score was significantly correlated with albumin, age, CRP, oxygen saturation, severity of diseases, LOS, admission to an ICU, and mortality (Table 3).

When the factors affecting the mortality were evaluated with cox regression analysis, albumin and CRP level was found statistically, NRS-2002 test, age, O_2 saturation, and severity of diseases were not found (Table 4).

Table 1. The characteristics of cases with and without nutritional risk according to NRS-2002

	NRS-2002 <3 (n=131)	NRS-2002 ≥3 (n=11)	p value
Age (mean)	54.2±11.4	65.7±13.5	0.02
LOS (day)	10.2±5.1	11.8±13.3.1	0.40
Mortality +/-	5 (3.8%)/126 (96.1%)	6 (54.5%)/5 (45.4%)	0.001
ICU need +/-	4 (3%)/127 (97%)	9 (95.3%)/2 (4.6%)	0.001
Mean of BMI	27.6±4.5	28.2±5.9	0.40
Sex M:F	77 (58.7%)/54 (41.2%)	5 (45.4%)/6 (54.5%)	0.39
Albumin (g/L)	41.6±3.7	36.1±0.6	0.64
Age 65 (below/above)	98/33 (96.1%-82.5%)	4/7 (3.9%-17.5%)	0.001
Class of BMI			
Healthy (n=56)	52 (39.7%)	4 (36.4%)	0.81
Overweight (n=86)	79 (60.3%)	7 (63.6%)	

LOS: Length of stay, ICU: Intensive care unit, M: Male, F: Female, BMI: Body mass index, NRS: Nutritional risk screening

Discussion

We performed a nutrition risk evaluation with the NRS-2002 test in non-critical COVID-19 patients in our study. 7.7% of patients were found with a nutritional risk. The patients with NRS-2002 score ≥3 had an older age and higher mortality and admission to the ICU than NRS-2002 score <3.

In our study, DM was found in one of the five patients followed up with the diagnosis of non-critical COVID-19 pneumonia, and obesity was found in one of the three patients. The patients with a normal BMI ve even obese patients had a nutritional risk. The evaluation of the nutritional status of the patients is crucial because malnutrition increases the infection risk (12).

MNA, subjective global ass (SGA), MUST, and NRS-2002 were designed to evaluate the nutritional risk. MUST has been used mostly as a screening test. SGA, MNA, and NRS-2002 were assessed in hospitalized patients. NRS-2002 test is remarkable with a design to perform easier and faster than other tests. The NRS-2002 test was validated by the ESPEN and suggested for NRS-2002 of hospitalized COVID-19 patients (8,13). Furthermore NRS-2002 was showed as a valid and reliable test in hospitalized patients in a thesis study in our country (14).

In previous studies, although the nutritional risk ratios were found to be lower according to NRS-2002 compared with tests such as MUST and MNA-SF, NRS-2002 was reported to be more effective in predicting the clinical outcomes of the nutritional status of the patients (15).

A nutritional risk for 77-92% was reported in studies which were performed with the NRS-2002 test in COVID-19 pneumonia and those findings were evaluated to be related to the high amount of old patients (16,17). The NRS-2002 test had a high sensitivity and low specificity to predict the LOS and the need of ICU in COVID-19 patients (16).

Table 2. The comparison of mortality and survival of the cases

	Non-survivor (n=11)	Survivor (n=131)	p value
NRS-2002	2.64±1.7	0.87±0.9	0.001
Age (mean)	66.4±13.1	54.2±16.4	0.01
BMI (mean)	25.5±5.1	27.2±4.6	0.23 NS
Sex M:F	8/3	74/57	0.29 NS
Weight	70.3±12.7	77.3±15.4	0.14 NS
Median of CRP (mg/L)	164±102.5	60.9±65.3	0.001
Age 65 (below/above)	5/6 (4.9%/15.0%)	97/34 (95.1%/85%)	0.04
O_2 saturation % (room air)	85.0±6.6	92.8±3.9	0.001
Mean of albumin (g/L)	28.7±8.0	39.0±4.9	0.001
DM +/-	3/8 (27.3%/76.6%)	28/103 (21.4%/ 78.5%)	0.64 NS
Obesity +/-	9/2 (81.8%/18.1%)	70/59 (54.3%/45.6%)	0.07 NS
Severity of diseases +/-	10/1 (32.3/0.9%)	21/110 (67.7/99.1%)	0.000

BMI: Body mass index, CRP: C-reactive protein, NRS: Nutritional risk screening, NS: Non-significant, M: Male, F: Female, DM: Diabetes mellitus

Table 3. The correlation of NRS-2002 score with clinical and laboratory parameters

Variable	Correlation with NRS-2002	p value	
Age	0.401	0.000	S
Albumin	-0.277	0.001	S
BMI	-0.153	0.70	NS
CRP	0.236	0.05	S
O_2 saturation (air room)	-0.618	0.001	S
Severity of diseases	0.579	0.001	S
LOS (length of stay)	0.200	0.018	S
ICU	-0.590	0.001	S
Mortality	-0.420	0.001	S

S: Significant, NS: Non-significant, BMI: Body mass index, CRP: C-reactive protein, LOS: Length of stay, ICU: Intensive care unit, NRS: Nutritional risk screening

Table 4. The evaluation of factors affecting mortality according to cox regression analysis

Variable	B	SE	Wald	Df	Sig	Exp (ß)	95% CI (min-max)	
Albumin	-0.209	0.089	5.50	1	0.019	0.812	0.682	0.966
CRP	0.017	0.008	4.68	1	0.030	1.01	1.00	1.03
Age	0.056	0.118	0.227	1	0.634	1.05	0.839	1.33
Oxygen saturation	-0.033	0.149	0.049	1	0.825	0.968	0.723	1.29
NRS-2002	0.020	1.57	0.000	1	0.990	1.02	0.047	22.12
Severity of diseases	0.045	1.02	0.193	1	0.661	1.57	0.209	11.79

CRP: C-reactive protein, NRS: Nutritional risk screening, CI: Confidence interval, SE: Standard error, Df: Degrees of freedom

In our study, our nutritional risk rate was found to be 7.7%, lower than that reported in the literature. We think that this migth be due to the younger average age of our patient group and the fact that the patients were screened for malnutrition with the NRS-2002 test at admission and the test was not repeated during hospitalization.

In a study conducted on 182 patients over 65 years of age with COVID-19 pneumonia, the risk of malnutrition was found to be 27.5% and to be associated with DM, albumin level, and arm circumference measurement (9). In our study, the nutritional risk rate was found to be 17% in the group over 65 years of age and it was 5 times higher than the group under 65 years of age. Higher predisposition to infections due to the increasing malnutrition risk with older age and impaired immune functions is been known.

Furthermore older age was reported as a risk factor in COVID-19 patients in many studies. Factors affecting the prognosis in COVID-19 pneumonia are reported as advanced age, DM and male gender, and obesity (6). The prevalence of obesity in COVID-19 patients varies between 10-75.8% in studies. Obese patients infected with COVID-19 required more ICU admission and longer hospital stay (5). In our study, our DM rate was 21.8% and our obesity rate was 23%. Although the rate of underweight cases was very low, the rate of obesity was compatible with the literature. We found that there was a nutritional risk not only in patients with normal weight but also in obese patients but DM and obesity were not found to be significant in terms of nutritional risk and mortality.

In this study, the average age, need for ICU admission, and mortality in the nutritional risk group were higher than the group without the nutritional risk. The sex, length of hospital stays, and BMI were not different between the two groups. There was no difference between the groups with and without the nutritional risk in terms of the length of the hospitalization stay rates. We think that it migth be due to the reasons that COVID-19 pneumonia is an acute disease, the rapid progression of the patients, and their discharge to ICU or death may have affected the hospitalization days.

In our study, the mean of BMI and weight of the cases were lower in the non-survivor patients than in the survivor group; however, but the difference was not significant statistically. Also, the sex distribution was not different between the dead and alive patients.

NRS-2002 scores of the patients who died were higher than those who survived, their albumin and oxygen saturation levels were lower, and CRP values were higher. Differences between the groups were statistically significant. Serum albumin level alone may sufficiently reflect malnutrition in hospitalized COVID-19 patients, especially in highly vulnerable individuals (13). Serum albumin level and CRP were reported as independent risk factors for mortality in COVID-19 patients, and an odd ratio was found 0.94 and 1.006 respectively (18). In our study, albumin levels were significantly lower in non-survived patients. Hypoalbuminemia was associated with a poor prognosis of COVID-19 (16). Even the mechanism is unclear, hypoalbuminemia was thought to be caused by increased capillary permeability and liver damage because of the cytokine storm (19).

In a study of elderly hospitalized patients in Brazil, NRS-2002 was found to be more effective than MNA and a MUST in predicting mortality, and it was reported as area under the curve (AUC): 0.78 for death (15). In another study, AUC was reported to be 0.86 to predict death for NRS-2002 (20). The prognostic value of NRS-2002 has been investigated in cancer, COPD, and critical illness (21). NRS-2002 was found to be more effective in predicting clinical prognosis and mortality.

Malnutrition was associated with disease progression and ICU need and mortality in hospitalized patients with COVID-19 pneumonia (11,13).

The NRS-2002 score was significantly correlated with albumin, age, CRP, oxygen saturation, severity of diseases, LOS, admission to an ICU, and mortality. Besides the factors affecting the mortality were evaluated with cox regression

analysis and albumin and CRP level were found statistically, NRS-2002 test, age, oxygen saturation, and severity of diseases were not found.

Many risk factors affect their nutritional status. It has been reported that factors such as socio-economic status, daily dietary intake and lifestyle, exposure to viral load, and time of initiation of treatment affect the nutritional status of patients with COVID patients (16). Since we did not evaluate the nutritional habits of the patients before hospitalization, the gastrointestinal tract symptoms due to viral load, and the side effects of the drugs used in our study, we cannot make any implications about the effect on nutritional risk. Nutrition is a dynamic process, and since the NRS-2002 evaluation is made within the first 24 h of hospitalization, we do not know whether a risk develops in the following days in patients who are not at risk, we think that these reasons have affected our results. Our study was conducted during the first wave of the pandemic, and the majority of the patients had mild-to-moderate infection. We think that the NRS-2002 test may have reduced its effectiveness in evaluating the prognosis of patients with COVID-19 pneumonia.

Malnutrition, frequently overlooked, is defined simply as imbalanced feeding, under or over feeding, and affects both thin and obese people. It is commonly seen in hospitalized patients, affects the prognosis adversely, increases both hospital stay and costs (20). Our results showed that the coexistence of advanced age and nutritional risk as a negative prognostic factor was supported by the finding of high nutritional risk and increased mean age in the non-survivor cases. Even our study did not show any association between the NRS-2002 score and mortality and admission to ICU in non-critical COVID-19 pneumonia, the NRS-2002 score was significantly correlated with albumin, age, CRP, oxygen saturation, severity of diseases, LOS, admission to an ICU, and mortality.

The limitations of the study, single-center and retrospective design of the study, limited data about the physical activity and eating habits affecting the nutritional status of the cases, and evaluation of sarcopenia with BMI. Furthermore, nutritional support products were not assessed because they were excluded from the study. Also, due to the sample size of the study, which was relatively small, our findings could not be generalized to all hospitalized patients.

Despite its limitations, we think that the use of NRS-2002, which is a non-invaziv method with lower costs to assess the nutritional risk of COVID-19, helps contribute to the prognosis of the disease.

As a conclusion, the results indicated that the use of the NRS-2002 test in cases with COVID-19 pneumonia was very helpful to assess the need for ICU and mortality. It should be the first step to assess risky patients, especially the elderly and those having acute or chronic diseases. Malnutrition seems to be a problem for viral pandemics in the 21st century and after.

In the future, in a viral pandemic, we might confront a problem named two-sided malnutrition, under and overfeeding, which aggravates the severity of the disease. More studies with nutritional support products are needed.

Study Limitations

The limitations of our study were the single-center setting and retrospective study design as well as the absence of data about physical activity and eating habits of patients, which might have affected the nutritional status of the cases and of evaluation for sarcopenia in addition to BMI. Furthermore, we did not collect information about the use of nutritional support products in our study. Because to the relatively small size of our patient population, our findings can not be generalized. Overall, our results showed that NRS-2002 helped predict the need for ICU admission and the risk of mortality in COVID-19 pneumonia, particularly in older patients.

Conclusion

We suggest that a simple, user-friendly NRS-2002 tool should be performed to evaluate the nutritional risk in COVID-19 pneumonia in routine clinical assessments. Performing NRS-2002 more than once in the hospitalization process may help the physicians in the early treatment of malnutrition and improve the prognosis of the disease.

Ethics

Ethics Committee Approval: This study was approved by the University of Health Sciences Turkey, Istanbul Training and Research Hospital Ethical Committee (12.06.2020-2400).

Informed Consent: An informed consent form was signed by each patient included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.B., B.P.Y., Design: A.B., B.P.Y., H.A., C.A., Data Collection or Processing: A.B., B.P.Y., H.A., Analysis or Interpretation: A.B., B.P.Y., A.D.A., C.A., Literature Search: A.D.A., C.A., Writing: A.B., B.P.Y., C.A.

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The Health Literacy and Health-seeking Behavior of Patients with a Chronic Disease Requiring Hospitalization

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What is known on this subject?

Health literacy and health-seeking behavior in people with chronic illness.

What this study adds?

In the debate on diving health inequalities, health knowledge (HL) has been conceded by the World Health Organization as a crucial determinant of health and good. Rapid development of coronavirus disease-2019 (COVID-19) into a epidemic has called for people to acquire and apply health information, and acclimatize their geste at a fast pace. HL and health-seeking behaviours should concentrate on; perfecting the quality of health communication that reaches a diversity of populations, especially by perfecting frontline professional chops and suppor, enabling people to develop transmittable chops in penetrating, understanding, assaying, and applying health information; and icing that precedence is propor tionate to need by reaching and engaging the population groups who are disproportionately affected by low HL.

ABSTRACT

Objective: Health literacy is a broad term encompassing how an individual obtains, understands, evaluates and applies correct health information for a disability-free life and to be able to maintain quality of life in sickness and in health throughout their lifetime. The sources of correct information and health literacy are important factors in being able to achieve the successful management of chronic diseases in particular. This study aimed to examine the relationship between health literacy and health-seeking behaviors and the characteristics of patients with a chronic disease requiring hospitalization.

Material and Methods: The study sample was formed of 194 patients, aged >18 years, treated in the internal medicine clinics of training and research hospital in Istanbul between 1 February and March 30, 2022. Data were collected using a questionnaire consisting of 3 sections. In the statistical analysis, IBM SPSS vn. 23.0 software was used.

Results: A significant negative relationship was determined between health literacy and health-seeking behaviors and age and education level of the demographic characteristics ($p<0.05$). Online health-seeking behavior was determined to be lower in patients with cardiac and chest diseases, and health-seeking behavior was seen to be higher on the first hospitalization ($p<0.05$).

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Conclusion: It can be considered that studies related to the health literacy and health-seeking behaviors of patients with a chronic disease will be an important source for disease management, enabling patients to lead a disability-free life.

Keywords: Health, literacy intervention, seeking behavior, chronic disease

Introduction

Information and education are basic rights of all healthy and sick individuals in society. In this respect, health literacy is a broad term encompassing how an individual obtains, understands, evaluates and applies correct health information for a disability-free life and to be able to maintain quality of life in sickness and in health throughout their lifetime (1). The United States of America Health and Human Services Department have stated that the target for 2030 is that "health literacy occurs when services are provided that will enable easy access to correct health information that can be understood and used, which will affect people's decisions and actions". This goal emphasizes the need to focus on both those who transmit information and those who seek information in the effective dissemination of health information (2).

Chronic diseases are diseases that tend to be long-term, originating from a combination of non-contagious genetic, physiological, environmental, and behavioral factors. A lack of information or incorrect information in chronic disease conditions not only limits the efficacy of treatment but also has a negative effect on self-care and quality of life. Patients with chronic diseases seek health information more on subjects related to drug information, nutrition, disease management, and disease preventative activities. Access to this information is usually currently obtained from healthcare professionals through online or traditional routes. Studies in the literature related to health literacy conducted on patients with chronic diseases have consistently stated that e-health interventions for individuals with chronic diseases have a significant effect on increasing patient participation in and self-management of healthcare services (3).

To be able to maintain quality of life and a disability-free life, especially in chronic diseases, information sharing related to health literacy is a two-way process requiring communication skills to know which questions to ask and which information to share, for the information recipient to be able to access and understand the shared information, and to be able to make the right decision related to the information and put it into practice. Therefore, the healthcare provider has the responsibility to transmit accurate information and the patient to be an active participant in care.

From this starting point, healthcare professionals play a crucial part in promoting health knowledge in cases to help them pierce the healthcare system effectively. This includes helping patients to find, understand, and evaluate health information. Healthcare professionals should evaluate the health literacy needs of patients and check the understanding of the patient for communication of sufficient health information (4).

This study aimed to examine the relationship between health literacy and health-seeking behaviors and the demographic and disease-related characteristics of patients with a chronic disease requiring hospitalization.

Material and Methods

Study Universe and Sample

The study universe was formed of patients treated in the internal medicine clinics of training and research hospital in Istanbul between 1 February and March 30, 2022. Repeated hospitalizations were discounted, and from a total of 364 patients, a minimum sample size of 170 patients was determined from the results of the G*Power 3.1 analysis. The study sample consisted of 194 patients aged >18 years who agreed to participate in the study.

Data Collection Tools

A questionnaire of 3 sections was used for data collection purposes in this study. In the first section, the participants were asked questions to elicit personal and disease-related information. The second section of the questionnaire consisted of the health literacy scale, which was tested for validity and reliability in Turkish by Aras and Bayık Temel (5). This scale consists of 25 items in 4 subscales of access to information (1-5), understanding information (6-12), evaluation (13-20), and application/use (21-25) (5). The internal consistency coefficient (Cronbach alpha) of the health literacy scale has been reported to be 0.92. The third section of the questionnaire comprised the health-seeking behaviour scale, which was developed by Kıraç and Öztürk (6). This scale consists of 12 items in 3 subscales of online search, traditional search, and professional search (6). The internal consistency coefficient (Cronbach alpha) of the health-seeking behaviour scale has been reported to be 0.83.

Authorization for the study was attained from the Ethics Committee of University of Health Sciences Turkey, Umraniye Training and Research Hospital (decision no: 1741, dated: 11.01.2021). Written informed consent for participation in the study was obtained from all patients.

Statistical Analysis

Data obtained in the study were analyzed statistically using IBM SPSS vn. 23.0 software. Descriptive statistical methods were used with continuous data reported as mean ± standard deviation values and categorical data as number (n) and percentage (%). The independent samples t-test, variance tests, and correlation analyses were also used.

Results

The demographic characteristics and disease-related information of the patients hospitalized and treated in the internal clinics are shown in Table 1.

The evaluation was made of 194 patients, comprising 99 (51%) females and 95 (49%) males with a mean age of 57.12±15.71 years. Of the total patients, 125 (64.4%) were married, 124 (63.9%) had a primary school level of education, and 75 (38.7%) were not employed. The hospitalization data were examined and it was seen that 70 (36.1%) were hospitalized in the internal medicine clinic, 96 (49.5%) had been diagnosed within the last year, and 74 (38.1%) had been hospitalized once in the last year (Table 2).

The relationships were examined between the demographic characteristics of the patients and the subscales of the Health Literacy Scale.

A negative correlation was determined between age and the subscales, at a level of statistical significance for access to information (-0.286*) and understanding information (-0.314*).

The access to information, evaluation, and application points of females were higher than those of males, and the understanding information points of males were higher than those of females, but the differences were not statistically significant. The health literacy subscale points of single patients were lower than those of the patients who were married or divorced, but not at a level of statistical significance.

In the evaluation of education level, the health literacy subscale points of the patients with a high school or further education level were seen to be higher, and in the understanding information subscale, the points of the patients with a primary school level of education (10.31±6.53) were determined to be statistically significantly lower (p=0.000*).

Clerical workers were seen to have high points in the access to information subscale, manual workers had low points in the evaluation subscale, and retired patients had low points in the application subscale. The understanding information subscale points of the unemployed patients (9.76±6.26) were determined to be statistically significantly low (p=0.000*).

Patients hospitalized in the chest diseases clinic were determined to have lower health literacy subscale points than

Table 1. The demographic characteristics and disease-related information of the patients hospitalized and treated in the internal clinics

Age (years)	57.12 (18-91)	SD 15.71	
		N	%
Gender	**Female**	99	51.0
	Male	95	49.0
Marital status	**Married**	125	64.4
	Single	59	30.4
	Divorced	10	5.2
Education level	**Primary school**	124	63.9
	High school	43	22.2
	Further education	27	13.9
Occupation	**Unemployed**	75	38.7
	Manual worker	27	13.9
	Retired	20	10.3
	Clerical worker	34	17.5
	Self-employed	38	19.6
Clinic in which hospitalized	**Internal**	70	36.1
	Nephrology/endocrine	28	14.4
	Cardiology	22	11.3
	Onco-hemato	13	6.7
	Chest diseases	26	13.4
	Neurology	20	10.3
	Dermatology	15	7.7
Time since diagnosis	**0-1 year**	96	49.5
	2-3 years	35	18.0
	4-5 years	22	11.3
	6-7 years	7	3.6
	8 years	34	17.5
Number of hospitalizations in the last year	**First hospitalization**	35	18.0
	1	74	38.1
	2	47	24.2
	3	22	11.3
	4	8	4.1
	5	8	4.1

SD: Standard deviation

Table 2. The relationships of the demographic characteristics and disease-related information of the patients with the health literacy scale points

Health literacy		Access to information		Understanding information		Evaluation		Application	
Age		**-0.286***		**-0.314***		-0.065		-0.116	
Gender	**Female**	19.16±6.25		11.49±6.85		11.21±4.30		9.04±4.13	
	Male	19.13±5.76		13.23±7.18		10.99±3.99		8.85±4.20	
	t p	0.041	0.97	-1.724	0.09	0.374	0.71	0.314	0.75
Marital status	**Married**	19.30±6.33		12.27±7.32		11.34±4.16		8.87±4.41	
	Single	18.71±5.20		12.25±6.60		10.66±4.08		8.97±3.73	
	Divorced	19.70±6.62		13.80±6.68		10.80±4.49		9.80±3.43	
	F p	0.239	0.788	0.223	0.801	0.558	0.573	0.230	0.795
Education level	**Primary school**	18.40±6.44		10.31±6.53		11.31±4.24		8.81±4.32	
	High school	20.49±4.23		16.67±6.78		10.91±3.73		9.23±4.06	
	Further education	20.41±5.90		14.78±5.98		10.48±4.35		9.11±3.63	
	F p	2.670	0.72	17.382	**0.000***	0.500	0.608	0.184	0.832
Occupation	**Unemployed**	18.44±6.67		9.76±6.26		11.64±4.29		9.23±4.40	
	Manual worker	19.22±6.82		12.19±6.87		9.07±4.85		9.04±4.23	
	Clerical worker	20.85±3.45		13.70±7.04		11.50±2.65		8.25±4.42	
	Retired	19.82±4.32		14.06±6.81		11.24±3.60		7.91±3.04	
	Self-employed	18.97±6.33		15.32±7.38		11.16±4.15		9.63±4.31	
	F p	0.777	0.54	5.339	**0.000***	2.036	0.09	1.015	0.401
Clinic in which hospitalized	**Internal**	17.43±6.52		24.74±7.95		28.84±9.47		18.81±6.13	
	Nephrology/endocrine	17.82±7.50		24.96±8.53		29.36±12.15		19.07±7.76	
	Cardiology	18.05±3.84		24.73±2.73		27.86±3.50		19.81±1.59	
	Onco-hemato	19.15±5.29		24.85±7.44		31.08±8.29		19.62±5.19	
	Chest diseases	16.23±6.38		22.46±8.18		27.42±10.37		18.00±6.25	
	Neurology	18.80±7.30		26.60±9.20		30.35±10.38		19.40±7.34	
	Dermatology	19.73±6.96		27.13±8.74		31.60±9.97		22.00±3.57	
	F p	0.698	0.652	0.764	5.83	0.518	0.794	0.774	0.591
Time since diagnosis	**0-1 year**	18.79±6.01		26.27±6.78		30.29±8.32		19.79±5.25	
	2-3 years	18.54±6.50		24.60±8.48		28.86±10.14		18.06±6.79	
	4-5 years	16.41±7.22		22.82±9.48		26.32±11.81		18.50±7.08	
	6-7 years	15.86±7.93		23.29±10.50		24.71±10.53		16.14±8.17	
	8 years	15.71±6.31		22.74±7.72		28.88±10.38		19.47±5.90	
	F p	2.048	0.09	1.901	0.11	1.220	0.30	1.096	0.36
Number of hospitalizations in the last year	**First hospitalization**	20.83±5.63		29.71±5.32		33.94±6.57		21.57±4.54	
	1	17.84±6.09		24.41±7.77		28.49±9.22		19.08±5.70	
	2	16.74±6.57		23.48±7.77		28.64±9.66		18.55±5.93	
	3	15.32±6.96		21.18±8.39		24.86±11.09		17.18±7.58	
	4	17.50±7.98		23.25±9.05		27.13±12.09		17.13±6.66	
	5	18.25±5.85		27.75±6.23		30.75±10.63		20.00±7.46	
	F p	2.573	**0.03***	4.769	**0.00***	3.002	**0.012***	1.972	0.08

**p<0.05*

patients in the other internal disease clinics, but the difference was not statistically significant.

When the relationship was examined between health literacy and the time since diagnosis and the number of hospitalizations within the last year, the health literacy subscale points were determined to be higher for those in the first year of diagnosis and in the first hospitalization, but not at a statistically significant level. A statistically significant difference was determined between the first hospitalization and seeking health literacy information (20.83±5.63, 0.03*), understanding information (29.71±5.32, 0.00*), and evaluation (33.94±6.57, 0.012*) (Table 3).

The relationships were examined between the demographic characteristics of the patients and the subscales of the health-seeking behaviour scale.

A statistically significant negative correlation was determined between age and online (-0.363*), professional (-0.339*), and traditional (-0.324*) health-seeking behaviors.

The traditional health-seeking behavior of males and females was seen to be similar, and the online and professional health-seeking behaviors of males were determined to be higher than those of females, but not at a statistically significant level.

According to marital status, the online and professional health-seeking behaviors were determined to be higher than those of the single and married patients, and the traditional health-seeking behavior of married patients was higher, but the differences were not statistically significant.

When education level was evaluated, the online (16.64±6.57, 0.002*), professional (23.14±8.41, 0.000*), and traditional (27.53±10.26, 0.007*) health-seeking behavior points of the patients with a primary school level of education were determined to be statistically significantly low.

No statistically significant difference was determined in the health-seeking behaviors according to occupation, but the points in all subscales were lower in the unemployed group.

The relationships were examined between the clinics in which the patients were hospitalized and the health-seeking behaviors. The online health-seeking behavior points were determined to be the lowest in the patients hospitalized in the cardiology and chest diseases clinics and highest in the dermatology clinic (0.004*), and the difference was statistically significant. The professional and traditional health-seeking behavior was higher but not statistically significant in the patients hospitalized in the dermatology clinic. No statistically significant difference was determined in health-seeking behavior according to the time since diagnosis and number of hospitalizations. No direct or inverse increase or decrease was observed proportional to the time since diagnosis or the number of hospitalizations.

Discussion

Health literacy has become more important in the healthcare agenda both in European countries and in Turkey with the understanding of the inclusion of the role and responsibilities in individual health and the healthcare sector, and this has increased interest in the concept of health literacy. In nationwide studies of health literacy in European countries, it has been reported that of 9007 (57.3%) respondents to a health literacy questionnaire, approximately 4 of every 10 respondents had experienced difficulties in accessing, understanding, evaluating, and applying health information (7).

In the Health Literacy Level and Related Factors Research conducted in 2018 by the Ministry of Health General Directorate for Health Development in Turkey, it was reported that 7 of every 10 individuals had a health literacy level that was insufficient or borderline (8).

In many studies on health literacy, as in the current study, a negative relationship has been reported between age and health literacy, and it has been stated that the level of education and socioeconomic status are the most significant determinants of the health literacy level (9). When studies conducted after 2020 were examined, it was seen that in a study in Germany of 2151 participants aged >18 years, the health literacy of those aged ≥76 years was low, and a low level of health literacy was associated with a low level of education and low socioeconomic status (10). Similarly, in a study in Vietnam of 300 individuals aged >55 years, a negative correlation was determined between age and health literacy (11).

In studies that have investigated health literacy and education and occupation, a strong correlation has been reported. In a study conducted with 2433 participants, low health literacy was associated with a lower level of education and low socioeconomic status, and individuals who completed further education were found to have a higher probability of a healthy life compared with those with a low level of education, and low socioeconomic status was associated with lower life expectancy and higher morbidity (12,13,14,15,16). In the current study, the level of education and occupation were determined to be positively correlated with health literacy, and with health-seeking behavior. Another study in the literature, which included 423 individuals evaluated health literacy in terms of e-health, and reported that further

Table 3. The relationships of the demographic characteristics and disease-related information of the patients with the health seeking behaviour scale points

			Online health-seeking behavior		Professional health-seeking behavior		Traditional health-seeking behavior	
Age			**-0.363***		**-0.339***		**-0.324***	
Gender	**Female**		17.52±6.67		24.67±8.17		29.18±10.03	
	Male		18.16±6.19		25.04±7.47		29.08±9.11	
	F	**p**	-0.695	0.49	-0.334	0.74	0.071	0.94
Marital status	**Married**		17.58±6.59		12.27±7.32		11.34±4.16	
	Single		18.10±6.10		12.25±6.60		10.66±4.08	
	Divorced		19.30±6.75		13.80±6.68		10.80±4.49	
	F	**p**	0.403	0.669	0.572	0.565	0.447	0.640
Education level	**Primary school**		16.64±6.57		23.14±8.41		27.53±10.26	
	High school		20.47±4.90		27.65±5.20		32.14±6.45	
	Further education		19.11±6.64		28.26±5.98		31.70±8.93	
	F	**p**	6.647	**0.002***	8.988	**0.000***	5.035	**0.007***
Occupation	**Unemployed**		16.37±6.93		23.11±8.51		27.56±10.66	
	Manual worker		19.19±6.42		24.96±8.51		29.37±10.28	
	Clerical worker		18.50±5.75		27.80±4.53		31.90±6.14	
	Retired		18.15±5.91		26.47±6.27		29.50±7.44	
	Self-employed		19.11±5.91		25.21±8.00		30.29±9.83	
	F	**p**	1.736	0.14	2.078	0.09	1.082	0.37
Clinic in which hospitalized	**Internal**		10.41±5.84		11.01±4.18		8.47±4.11	
	Nephrology/endocrine		14.57±5.52		11.57±4.38		9.68±4.21	
	Cardiology		10.27±6.80		11.82±2.32		8.91±4.05	
	Onco-hemato		15.62±8.23		10.92±4.05		9.54±3.97	
	Chest diseases		11.77±7.76		10.69±4.48		8.23±4.09	
	Neurology		14.00±6.46		9.70±4.80		9.15±3.82	
	Dermatology		16.20±7.08		12.33±4.20		10.33±5.22	
	F	**p**	3.305	**0.004***	0.820	0.555	0.751	0.609
Time since diagnosis	**0-1 year**		12.51±7.04		11.50±3.97		9.00±4.24	
	2-3 years		13.60±7.98		10.46±4.46		9.03±4.19	
	4-5 years		11.73±6.37		11.09±4.36		8.23±4.01	
	6-7 years		13.00±6.35		9.71±4.50		9.71±4.79	
	8 years		10.85±6.70		10.94±4.16		9.03±4.04	
	F	**p**	0.576	0.58	0.635	0.64	0.232	0.92
Number of hospitalizations in the last year	**First hospitalization**		13.54±7.13		12.03±4.27		9.46±4.23	
	1		11.45±6.89		11.03±3.99		8.43±4.23	
	2		13.30±7.19		11.11±4.01		9.96±3.85	
	3		12.36±7.29		11.05±4.04		8.82±4.15	
	4		9.50±6.21		9.13±5.00		6.75±4.43	
	5		12.63±7.67		9.88±5.30		8.13±4.02	
	F	**p**	0.499	0.50	0.859	0.51	1.418	0.22

*$p<0.05$

education, working as a civil servant, and high income had a positive effect on e-health literacy (17,18).

Previous studies conducted with patients have shown that patients with chronic disorders have a lower level of health literacy, and patients with cardiovascular and chest diseases in particular have more problems in understanding health information (19,20,21). Although there was no statistically significant difference between the clinics with respect to health literacy levels in the current study, as only patients in internal disease clinics were included, the health-seeking behavior points of patients hospitalized in the cardiology and chest diseases clinics were found to be low.

Patients with chronic diseases need health literacy beshouldhey need to understand more health information and read prescriptions accurately, and low health literacy is associated with poor control of chronic diseases, presentation at the emergency department, hospitalization, and increased mortality (10,22,23). In the current study, a negative correlation was determined between the health literacy level and the number of hospitalizations in the last year.

Conclusion

Although few, previous studies related to health literacy and chronic diseases have shown a relationship between the level of health literacy and the presence of a chronic disease, time since diagnosis, and the number of hospitalizations. It can be considered that studies related to the health literacy of patients with a chronic disease will be an important source to be able to provide disease management, quality of life, and a disability-free life.

Ethics

Ethics Committee Approval: Ethics Committee of University of Health Sciences Turkey, Umraniye Training and Research Hospital (decision no: 1741, dated: 11.01.2021).

Informed Consent: Written informed consent for participation in the study was obtained from all patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.A., A.Ö., Concept: F.A., A.Ö., Design: F.A., A.Ö., Data Collection or Processing: F.A., Analysis or Interpretation: F.A., Literature Search: F.A., A.Ö., Writing: F.A., A.Ö.

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ORIGINAL ARTICLE

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Rhinitis: A Risk Factor in Asthma Control?

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What is known on this subject?

Asthma is strongly linked to allergic rhinitis (AR). AR is a heterogeneous disorder that is characterized by a group of nasal symptoms. Some studies were conducted to show the worsening effect of rhinitis on asthma control, especially in children and in adult patients comparing the asthma control test (ACT) scores.

What this study adds?

We studied this aspect in adult patients with validated assessment tools and by separating the patients into groups defining AR severity according to visual analog scale and asthma control status according to ACT scores.

ABSTRACT

Objective: We studied the risk factor aspect of rhinitis in adult patients with asthma using validated assessment tools and separating the patients into groups defining rhinitis severity according to visual analog scale and asthma control status according to asthma control test (ACT) scores.

Material and Methods: Asthma is a disease that causes coughing, wheezing, and shortness of breath. It is characterized by variable and recurrent symptoms and reversible airflow obstruction. Allergic rhinitis (AR) is a disease characterized by symptoms like sneezing, itching, nasal congestion, and runny nose. Asthma is linked to AR. AR is diagnosed in 70-90% of the patients, and asthma symptoms are observed in 40-50% of the patients who are diagnosed with AR.

Results: Of 114 patients with asthma receiving treatment, 78.9% were female, and 64% had mild rhinitis symptoms. While 12.3% had diabetes mellitus (DM), 30.7% had hypertension (HT), and 14.9% had ischemic heart disease (IHD). Age, sex, DM, HT, IHD, exacerbation, and diagnosis time groups in the last year did not seem to cause a significant difference in ACT scores. The difference between the rhinitis groups in terms of ACT scores was statistically significant (F= 8.506, p=0.004, partial η^2=0.087). According to this result, 8.7% of the total variance asthma control could be explained by the severity of AR.

Conclusion: Severe symptoms of rhinitis are associated with asthma control. Therefore, the management of AR should be targeted in patients whose asthma control cannot be optimized.

Keywords: Asthma, allergic rhinitis, symptom control, quality of life

Introduction

Asthma is a chronic respiratory disease affecting children and adults that causes cough, wheezing, and shortness of breath. It presents with variable and recurrent symptoms and reversible airflow obstruction. Asthma is strongly linked to allergic rhinitis (AR) (1,2). AR is a heterogeneous disorder that is characterized by a group of nasal symptoms.

The "one airway, one disease" one airway, concept was first described by Grossman (3) in 1997. The upper respiratory tract consists of the nose, nasal cavity, pharynx, and larynx. The lower respiratory tract is composed of the trachea, bronchi, bronchioles, and alveoli. The embryological status of the lower and upper respiratory tract is the 4th anterior, which consists of a respiratory diverticulum formed in the ventral wall

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of the intestine. Histologically, the trachea is detailed and structurally similar.

It was found that 70-90% of asthma patients were diagnosed with AR, and 40-50% of patients with AR also had asthma symptoms (4,5). The AR and its impact on asthma (ARIA) guidelines recommend targeting the optimal control of asthma and AR simultaneously (6).

The asthma control test (ACT) is an assessment tool for the quality of life and symptom severity of patients with asthma patients (7). The visual analog scale (VAS) can also be used as an assessment tool for the symptom severity of patients with rhinitis (1,8).

Some studies have shown the worsening effect of AR on asthma control, especially in children (1) and in adult patients by comparing ACT scores (2). In this study, we studied this effect in adult patients with validated assessment tools and by separating the patients into groups defining AR severity according to VAS and asthma control status according to ACT scores.

Material and Methods

Patients

Our prospectively designed single-center study was performed in strong consistency with the ethical standards of the World Medical Association's Declaration of Helsinki and was approved by the Ethical Committee of Kirsehir Ahi Evran University Faculty of Medicine (date: 21.12.2021, approval number: 2021-21/205). An informed consent form was signed by each patient included in the study.

We included patients with asthma and rhinitis presenting to pulmonology outpatient clinics between 01.12.2021 and 01.06.2022. The symptoms of rhinitis were questioned for diagnosis. The prick test was not available in our clinics. The inclusion criteria were being diagnosed with asthma and rhinitis, being treated actively, and signing the informed consent form. Patients who did not agree to sign the informed consent form were excluded.

VAS and ACT scores were measured after treatment for 4 weeks the ARIA and Global Initiative for Asthma Strategy guidelines. The demographic data, ACT and VAS scores, asthma control status, and AR severity levels of the patients were recorded. According to ACT scores, 25 points are classified as complete control, 20-24 points are classified as partial control, and 19 or lower scores are classified as uncontrolled asthma. Then, considering the mean scores, the number of attacks in a year was divided into 2 categories, namely "never having an attack" and "having at least one attack".

Asthma Control Test

ACT was used as an assessment tool to evaluate asthma control after a 4-week treatment. Asthma control was evaluated by asking the following five questions that were answered on a scale of 1 to 5:

1) In the past 4 weeks, how frequently did your asthma keep you from getting as much done at work, school, and home?

2) During the past 4 weeks, how often have you had shortness of breath?

3) During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness, or pain) wake you up at night, or earlier than usual in the morning?

4) During the past 4 weeks, how often have you used a rescue inhaler or nebulizer medication (such as albuterol)?

5) How would you rate your asthma control during the past 4 weeks?

The validity and reliability of ACT were demonstrated by Schatz et al. (7).

Visual Analog Scale

VAS was a tool for evaluate the severity of AR symptoms. AR symptoms were evaluated on a scale of 0 to 10. The validity and reliability of VAS were tested and confirmed by Ciprandi et al. (9) VAS scores of 0-3 indicate mild rhinitis, while scores of 4-7 indicate moderate rhinitis, and scores of 8-10 indicate severe rhinitis.

Statistical Analysis

The sample size required for the study was calculated using the G*Power 3.1.1 program. For this, based on a medium effect size defined by Cohen (1988), which was 0.25 in the analysis of variance, a type I error rate of 0.05, and 80% power, the number of patients to be included was calculated as. One hundred fourteen patients were included in our study.

We analyzed the collected data using the SPSS 25.0 program. Frequency, percentage, mean, standard deviation, and minimum-maximum values were calculated as descriptive statistics. In the study, by calculating the Cronbach's alpha internal consistency coefficient for the total ACT scores and the ACT scores related to AR, sex, age, number of attacks, the duration of diagnosis, and presence of other chronic diseases [diabetes mellitus (DM), hypertension (HT), ischemic heart disease (IHD)] with separate groups (2x2x6x2x2x2x2x2), eight-way comparisons were made with the mixed-factor analysis of variance (Ten-Way mixed-factor ANOVA) method. In addition,

the interaction effects of asthma control status with the other ten independent variables were examined.

Results

It was determined that 78.9% of the 114 asthma patients were female, and 64% had mild rhinitis. While 12.3% had DM, 30.7% had HT, and 14.9% had IHD. The average age of the patients was 45.55±14.79, the mean number of asthma attacks in the last year among the patients was 0.17±0.88, and the mean duration of diagnosis was 6.60±6.30 years (Table 1).

The internal consistency coefficient of ACT was found to be 0.929, while the mean ACT score of the patients was 21.57±3.76. Considering the GINA steps, which are used to evaluate the severity of asthma, it was seen that the mean asthma severity score of the patients was 2.99±0.36 on a scale of 1 to 5. The patients were asked to evaluate their complaints regarding rhinitis using VAS, and a score between 0 and 10 was used. Because of this evaluation, the mean VAS score of the patients was found to be 1.99±1.91 (Table 2).

In this study, in which the control of asthma was evaluated, First, the total ACT scores of the patients were categorized for the ANOVA as recommended in the literature. The duration of diagnosis was similarly classified as 5 years and shorter and 6 years or longer, which is considered the mean cut-off point. The patients were categorized based on their age groups as 18-24, 25-34, 35-44, 45-54, 55-64, and 65 or older. The Levene's test result was found as $p>0.05$ ($p=0.887$) after the conversion of the continuous variables into categorical variables. It was determined that the variances were homogeneously distributed, and the data were then analyzed.

There was a statistically significant difference in the ACT scores between the rhinitis severity groups ($F=8.506$, $p=0.004$, partial $\eta^2=0.087$). According to this result, 8.7% of the total variance in asthma control could be explained by the severity of AR. The groups formed based on age, sex, DM presence, HT presence, IHD presence, exacerbation in the last year, and the duration of diagnosis did cause a significant difference in the ACT scores of the patients (Table 3).

Table 1. **The demographic data**

Parameters		n
Gender	Female	90
	Male	24
Allergic rhinitis	Mild	73
	Moderate and severe	41
DM	Yes	14
	No	100
HT	Yes	35
	No	79
IHD	Yes	17
	No	97
Total		114
Age	$\bar{X}$ ± SD: 45.55±14.79	min-max: 18-79
Number of exacerbations in last year	$\bar{X}$ ± SD: 0.17±0.88	min-max: 0-6
The duration of diagnosis (years)	$\bar{X}$ ± SD: 6.60±6.30	min-max: 1-30

DM: Diabetes mellitus, HT: Hypertension, IHD: Ischemic heart disease, $\bar{X}$: Median, SD: Standard deviation, min: Minimum, max: Maximum

Table 2. **Descriptive features of measurement tools**

	Min-max	$\bar{X}$ ± SD	Cronbach alpha
ACT	5-25	21.57±3.76	0.929
GINA step	2-5	2.99±0.36	-
VAS	0-7	1.99±1.91	-

ACT: Asthma control test, GINA step: Global initiative for asthma step, VAS: Visual analog scale, $\bar{X}$: Median, SD: Standard deviation, min: Minimum, max: Maximum

Although there was a statistically significant difference between the ACT scores of the rhinitis severity groups, there was no interaction-common effect of rhinitis severity with other independent variables (Table 3).

Discussion

We showed the worsening impact of rhinitis on asthma control. It can be concluded in general that rhinitis is a risk factor for poor asthma control. Our results were also consistent with the results of previous studies in the literature.

Several studies have shown the relationships between upper respiratory tract pathologies (10,11,12). Type 2 inflammation is a clinical key in pathological processes in asthma and rhinitis cases (13,14). The common inflammatory processes and histological structures lead to a strong link between these diseases, as well as the interaction of asthma control and rhinitis severity.

Emons et al. (1) conducted a study to validate an assessment tool named "CARATkids" in children with asthma and AR symptoms. One hundred and eleven patients were included in their study. Emons et al. (1) also recorded ACT and VAS scores in the next 3 visits of the patients, and they performed Spearman's correlation analyses. According to their results, it was concluded that AR was a risk factor for poor asthma control, and VAS and ACT scores were significantly correlated. In a prospectively designed observational study by Linhares et al. (15), similar results were found.

Our study differs from the aforementioned studies in terms of the age of the sample and data analysis methods. The abovementioned studies can contribute to our results on the strong link between asthma and rhinitis.

In a prospective multicenter study by Yasuo et al. (2), 157 patients with asthma were separated into two groups of patients with and those without rhinitis. The GINA steps of the patients in the group with rhinitis were significantly higher. In the group of patients with rhinitis, step 2 asthma rates were lower, and step 4 asthma rates were higher, while there was no statistically significant difference between.

The step 3 asthma rates of the two groups. The female sex was more prevalent than the male sex in both groups.

In this study, the severity of rhinitis was not recorded, but only the diagnosis was evaluated as a parameter and risk factor. Our results were consistent with the findings of Yasuo et al. (2). Furthermore, we separated the patients into groups based on the determination of their asthma control status and rhinitis using ACT and VAS scores. Most of our patients had GINA step 3 asthma, and most patients in our sample were female. The local epidemiological status of asthma and our patient profile were found to be similar. Yasuo et al. (2) also used VAS scores for asthma and found these scores higher in the rhinitis group, which was not a parameter in our study.

Table 3. Eight-way mixed factor analysis of variance in terms of ACT total score

Independent parameters	F	p	Partial η^2
Allergic rhinitis groups (2)	8.506	**0.004**	0.087
Gender groups (2)	0.372	0.543	0.004
Age groups (6)	0.810	0.546	0.044
DM groups (2)	0.125	0.725	0.001
HT groups (2)	0.006	0.938	0.000
IHD groups (2)	0.620	0.433	0.007
Number of exacerbations groups (2)	0.305	0.582	0.003
Duration of diagnosis groups (2)	0.788	0.377	0.009
Interactions			
Allergic rhinitis groups x gender groups (2x2)	1.157	0.285	0.013
Allergic rhinitis groups x age groups (2x6)	0.800	0.553	0.043
Allergic rhinitis groups x DM groups (2x2)	0.263	0.609	0.003
Allergic rhinitis groups x HT groups (2x2)	0.084	0.773	0.001
Allergic rhinitis groups x IHD groups (2x2)	1.212	0.274	0.013
Allergic rhinitis groups x number of exacerbations groups (2x2)	0.042	0.839	0.000
Allergic rhinitis groups x duration of diagnosis groups (2x2)	1.230	0.270	0.014

DM: Diabetes mellitus, HT: Hypertension, IHD: Ischemic heart disease

Study Limitations

Our results and sample size were consistent with those of the limited number of previous studies in the literature. Our study is remarkable with a better study design including methods such as the creation of patient groups according to asthma control and rhinitis severity.

Conclusion

There was a statistically significant difference in the ACT scores between the rhinitis groups. According to this result, 8.7% of the total variance in asthma control could be explained by the severity of AR. A higher severity of rhinitis was associated with poorer asthma control. Therefore, physicians should target the optimal control of asthma and rhinitis simultaneously.

Ethics

Ethics Committee Approval: Ethical Committee of Kirsehir Ahi Evran University Faculty of Medicine (date: 21.12.2021, approval number: 2021-21/205).

Informed Consent: An informed consent form was signed by each patient included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: C.A., N.Z., Design: C.A., N.Z., Analysis or Interpretation: C.A., N.Z., Writing: C.A., N.Z.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Concomitant Peripheral and Pulmonary Arterial Thromboembolism 35 Days After SARS-CoV-2 mRNA Vaccine

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What is known on this subject?

Although several European countries reported cases of thromboembolism accompanied by thrombocytopenia following ChAdOx1 (Oxford-AstraZeneca) vaccine, such an association was rarely reported after vaccination with BNT162b2 (Pfizer–BioNTech).

What this study adds?

We present the case of an otherwise healthy patient who developed concomitant acute limb ischemia and extensive pulmonary embolism following the first dose of BNT162b2 vaccine.

ABSTRACT

Although thromboembolism after ChAdOx1 vaccine has been extensively reported, this association was rarely reported after vaccination with BNT162b2. We present the case of an otherwise healthy patient who developed concomitant acute limb ischemia and extensive pulmonary embolism (PE) 35 days after the first dose of BNT162b2 vaccine. Fogarty balloon thrombectomy was performed using open femoral artery exposure, and limb perfusion was restored. Reperfusion strategies were not used for treating PE due to low risk on prognostic assessment. The patient made an uneventful recovery, and she was discharged home on postoperative day 5 on warfarin, and remains symptom-free in a 3-month follow-up. Even though thromboembolic events following BNT162b2 are very rare, concomitant venous and arterial thromboembolism may occur in patients as late as 35 days after vaccination. However, the risk of thromboembolism following BNT162b2 vaccination appears significantly lower compared with severe acute respiratory syndrome-coronavirus-2 infection itself.

Keywords: BNT162b2, coronavirus 2019, vaccination

CAM & SAKURA MEDICAL JOURNAL

Introduction

It has been well established that coronavirus disease-2019 (COVID-19), the multi-systemic disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is associated with venous and arterial thromboembolic events across multiple organ systems (1). SARS-CoV-2 vaccines reduce the rate of thromboembolism as they prevent symptomatic and severe disease (2). Although several European countries reported cases of thromboembolism accompanied by thrombocytopenia following ChAdOx1 (Oxford-AstraZeneca) vaccine, such an association was rarely reported after vaccination with BNT162b2 (Pfizer-BioNTech) (2,3,4). We present the case of an otherwise healthy patient who developed concomitant acute limb ischemia

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(ALI) and extensive pulmonary embolism (PE) following the first dose of BNT162b2 vaccine.

Case Report

A 62-year-old woman presented with dyspnea and a cold, painful left lower limb. Her medical past was insignificant except for a right total knee replacement that occurred 2 months ago. The patient had recovered from surgery and was already mobile. She had received the first dose of BNT162b2 mRNA vaccine 35 days before presentation. On physical examination, she was slightly tachypneic with normal blood pressure and heart rate. The electrocardiogram showed a sinus rhythm. Heart and lung sounds were normal. Her left lower extremity was cyanotic and cold with absent popliteal and pedal pulses, minimal sensory loss, and normal motor function. Doppler signals distal to the left femoral pulse were inaudible. Laboratory tests revealed normoxia, hypocapnia, a D-dimer level of 5.61 µg/mL (normal range <0.5 µg/mL), and a platelet count of 171,000 per µL. Computed tomography angiography of the lower extremities and pulmonary arterial system demonstrated thrombotic occlusion of the left external iliac artery (Figure 1) and bilateral PE (Figure 2). There were not any signs of right ventricular overload or dysfunction, intracardiac thrombi, or any septal defects on the transthoracic echocardiographic examination. Venous duplex ultrasound of the extremities was negative for deep vein thrombosis. A COVID-19 polymerase chain reaction test was also negative. The patient was immediately anticoagulated using unfractionated heparin, and transferred to the operating room for the surgical treatment of ALI. Fogarty balloon thrombectomy was performed using open femoral artery exposure, and limb perfusion was restored. Reperfusion strategies were not used for treating PE due to low risk on prognostic assessment. Genetic thrombophilia testing did not demonstrate an increased risk of thromboembolism. Lupus anticoagulant and anti-cardiolipin antibodies were negative. The patient made an uneventful recovery, and she was discharged home on postoperative day 5 on warfarin, and remains symptom-free in a 3-month follow-up.

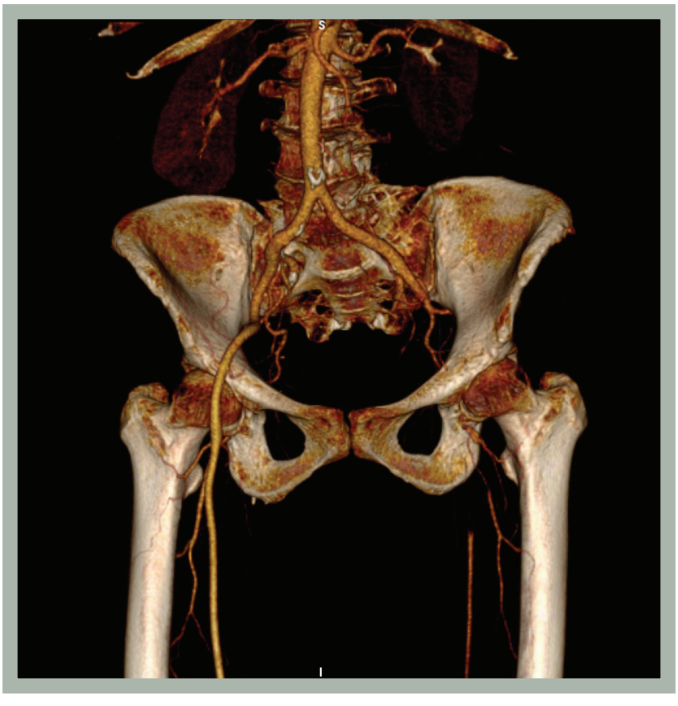

Figure 1. Three dimensional reconstruction of contrast enhanced computed tomography scan demonstrating left external iliac artery thrombosis

Discussion

The current report describes the occurrence of concomitant pulmonary and peripheral arterial thromboembolism following immunization with the BNT162b2 vaccine. There is no direct evidence that thromboembolic events observed in this particular patient were caused by vaccination; however, we failed to demonstrate any other causes of arterial and venous thromboembolism, such as a proximal source or genetic predisposition.

Thromboembolism after ChAdOx1 has been extensively reported, yet such association was rarely reported after BNT162b2 (2,3,4). A recent self-controlled case series study by Hippisley-Cox et al. (5) analyzed over 29 million people in England who received the first doses of ChAdOx1 or BNT162b2 mRNA vaccines and approximately 2 million people with a positive COVID-19 test. The outcomes were hospital admission or death associated with thrombocytopenia or

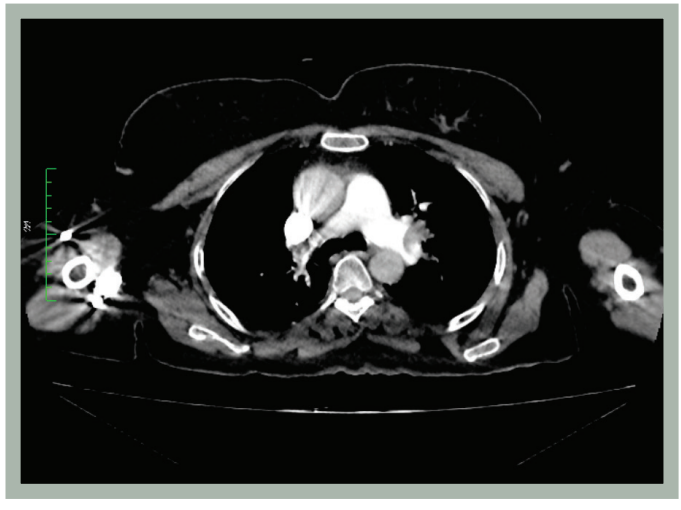

Figure 2. Contrast enhanced computed tomography scan demonstrating left main pulmonary artery thromboembolism

thromboembolism within 28 days of vaccination or COVID-19 infection. The authors reported that vaccination with ChAdOx1 was associated with increased risks of thrombocytopenia, venous thromboembolism, and rare arterial thromboembolic events. They also reported that vaccination with BNT162b2 increased the risk of arterial thromboembolism, and both vaccines increased the likelihood of cerebral venous sinus thrombosis. However, they also reported that all of the above-mentioned complications were more commonly observed and more prolonged after SARS-CoV-2 infection in the same population (5). Therefore, it can be interpreted that SARS-CoV-2 vaccination protects against thromboembolism during the COVID-19 pandemic.

Another study by Sessa et al. (6) included women ≤50 years of age and concluded that mRNA vaccines did not show disproportional reporting of thromboembolic events compared to hormonal contraception. Moreover, others reported that the risk of thromboembolism was not increased 14 days (7), 21 days (8), and 42 days (9) following immunization with BNT162b2. Considering the accumulating evidence, the European Medical Agency has stated that the benefits of vaccination against SARS-CoV-2 continue to outweigh the risk of side effects (10).

Even though thromboembolic events following BNT162b2 are very rare, concomitant venous and arterial thromboembolism may occur in patients as late as 35 days after vaccination. However, the risk of thromboembolism following BNT162b2 vaccination appears significantly lower compared with SARS-CoV-2 infection itself.

Take home messages

• Thromboembolic events may be rarely be observed following BNT162b2 vaccination.

• The risk of thromboembolism following BNT162b2 vaccination appears significantly lower compared with SARS-CoV-2 infection itself.

Ethics

Informed Consent: Informed consent has been obtained from the patient for publication of the case report and accompanying images.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.C.T., A.E., N.K., M.Y., Concept: A.C.T., A.E., N.K., M.Y., Design: A.C.T., A.E., N.K., M.Y., Data Collection or Processing: A.C.T., A.E., N.K., M.Y., Analysis or Interpretation: A.C.T., A.E., N.K., M.Y., Literature Search: A.C.T., A.E., N.K., M.Y., Writing: A.C.T., A.E., N.K., M.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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CSMJ

Functional Magnetic Imaging in a Case of Congenital Mirror Movement

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What is known on this subject?

Mirror movements are involuntary movements caused by synchronized mimicry of one side's voluntary muscle movements by the opposite limb's homologous muscles.

What this study adds?

We think that when such complaints are encountered, functional magnetic resonance imaging should primarily be kept in mind and preferred to show the etiopathology non-invasively.

ABSTRACT

Mirror movements are involuntary movements caused by synchronized mimicry of one side's voluntary muscle movements by the opposite limb's homologous muscles. We present a case of mirror movement, which is shown also with functional magnetic resonance imaging.

Keywords: Congenital, EMG, fuctional MRI, mirror

Introduction

Mirror movements are involuntary movements caused by synchronised mimicry of one side's voluntary muscle movements by opposite limb's homologous muscles. Mirror movements can be seen in all limbs but are mostly seen in the upper limbs, especially in hands (1,2). It is normal to see mirror movements among children before the age of 10 because myelination of corpus callosum has not been finished. Among adults, physiological mirror movements can sometimes be seen due to tiredness, intense physical activity, and age. However, persistence and repetition of these movements are considered abnormal (3,4).

There are two main mechanisms for the formation of mirror movements. The first one is abnormal tract of ipsilateral motor corticospinal pathway, and the second one is reduced transcallosal inhibition or increased transcallosal excitation. The etiopathology of mirror movements differs by being congenital or acquired (4). Congenital mirror movements can be physiological or pathological. Mild physiological mirror movements of childhood can frequently be seen due to incomplete development of corpus callosum. Congenital mirror movements generally begin in infancy or early childhood. Progression and fluctuations are unlikely. Frequently seen in the upper limbs, especially in the hands and fingers. Cause mild disability. Expected to disappear between ages seven and ten. Pathological mirror movements on the other hand are permanent. Can be seen with isolated or complex congenital syndromes (Kallmann's

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syndrome, Klippel-feil's syndrome, hypoxic ischemic damage, Usher's syndrome, congenital hemiplegia, Friedrich's ataxia) (5,6).

Acquired mirror movements can be seen with many neurodegenerative diseases such as Parkinson's disease and Corticobasal syndrome. Can also accompany stroke, cervico-medullary junction lesions, essential tremor, dystonia, and amyotrophic lateral sclerosis (1,2,4,7,8).

Case Report

Twenty-two-year-old male patient presented with involuntary contractions that were present in one hand while moving the other hand (Video 1). These complaints that were present for the last couple of years and progressing lately were preventing him to work. We found that there was no loss of consciousness and no involvement of the lower limb. And the patient had a normal neurological examination. Pre, peri, and postnatal backgrounds were normal. While being cognitively normal, the patient had slower motor development from the childhood and was also being monitored by endocrinology for hypogonadotropic hypogonadism diagnosis. While being the first of the two children, his parents had first -degree consanguineous marriage and the other child has auditory problems. On physical examination, contractions in the opposite hand were especially evident while making precise motor movements on one hand. Anosmia and hyposmia were absent in the patient. Cranial and cervical magnetic resonance imaging (MRI) were normal (Figure 1). In laboratory examination, routine tests (hemogram and biochemistry), thyroid function tests, vitamins A, E, and B12, selenium, copper, ceruloplasmin, and lead values were normal. ELISA tests (hepatitis, HIV, HbsAg, anti-Hbs, and HCV) were also negative. In electroneuromyography (EMG) while forearm's voluntary movements, EMG activities in similar muscle groups of the opposite limb were observed. Sensory and motor conduction examinations were normal. In terms of congenital and metabolic anomalies, optometrical and otolaryngological examinations were normal. In functional MRI, it was seen that contralateral cortical motor areas were activated when both, hand actively moved and the other hand contracted involuntarily (Figure 2).

Discussion

Mirror movements are mimicry of the opposite side's voluntary muscle movements, especially in the upper limb distal muscles (3). Among various movement disorders, it is not quite rare. Mirror movements can be problematic. To try to cope with this situation, patients might suppress the mirror movements by contracting the opposite side's antagonist muscles. But even so, mirror movements are disabling. Recognition of these movements is crucial for early diagnosis. Two general mechanisms are suggested for the formation of mirror movements. First: progression of the corticospinal tract of the primary motor cortex (M1) of the hand originating from the same hemisphere to the ipsilateral spinal cord without crossing. These abnormal ipsilateral pathways may be related to the diagonally branching corticospinal fibers. This is thought to be related to the dysfunction of the neural circuits that must operate contralaterally to the primary motor cortex to

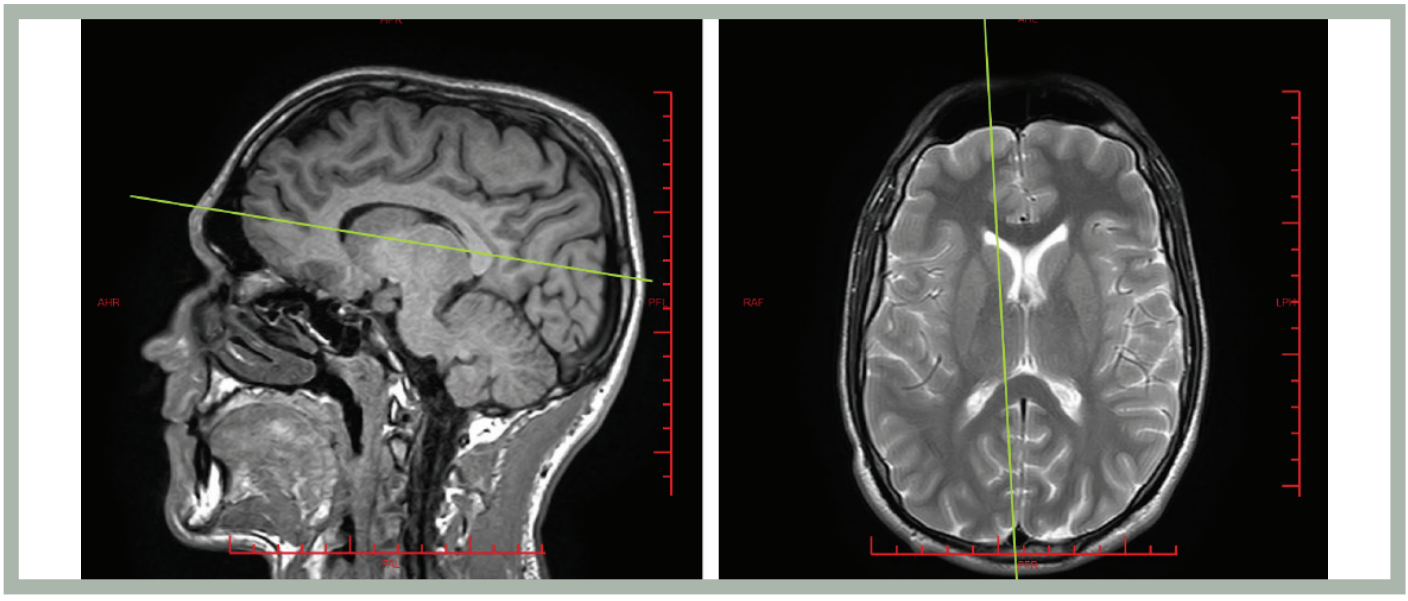

Figure 1. Cranial magnetic resonance imaging

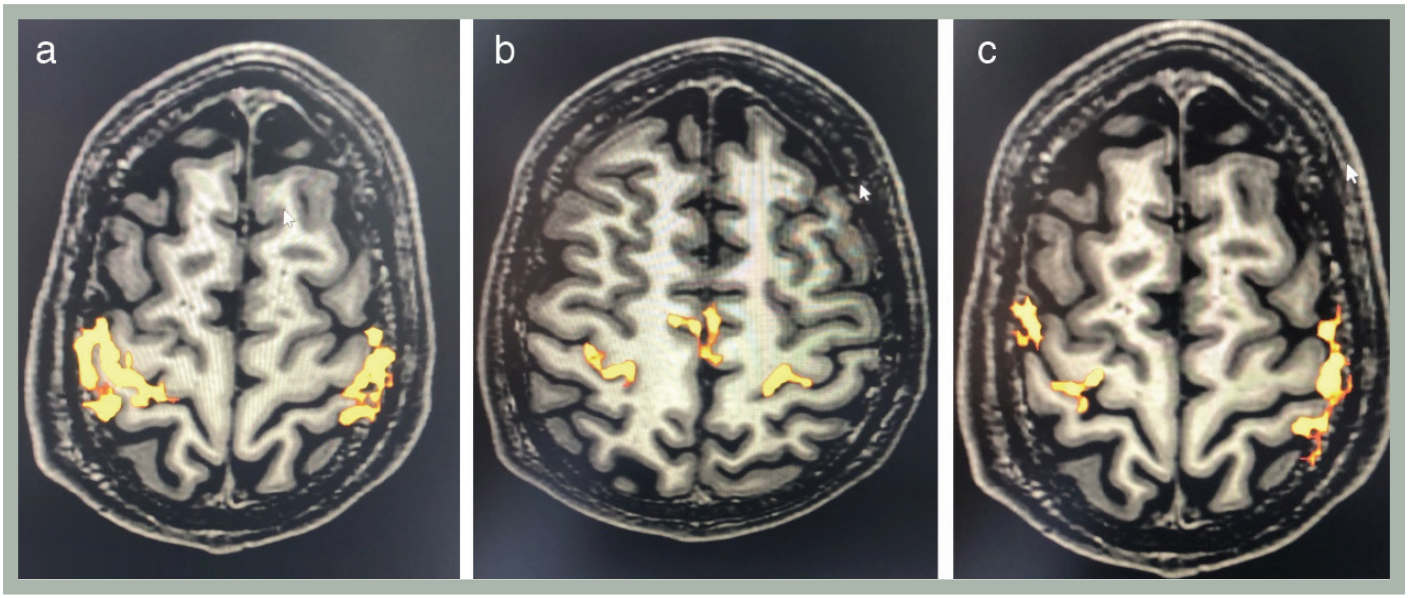

Figure 2. (a-c) In functional magnetic resonance imaging, it was seen that contralateral cortical motor areas were activated when both, hand actively moved and the other hand contracted involuntarily

which voluntary movement is dependent. Second: bilateral cortical activation due to decreased transcallosal inhibition or increased transcallosal excitation. As a result, mirror movements occur because of abnormal activation of both hemispheres of single-handed intended movements. The etiopathology of mirror movements provides clues about the congenital or acquired form of the disease (2,4).

Our case was evaluated primarily in terms of Kallmann's syndrome, due to mirror movements and the diagnosis of hypogonadotropic hypogonadism. Kallmann's syndrome is a neuronal migration disorder characterized by anosmia/hyposmia and hypogonadotropic hypogonadism. The clinical spectrum of isolated gonadotropin-releasing hormone deficiency includes various disorders, including Kallmann's syndrome, i.e., hypogonadotropic hypogonadism with anosmia, and its normosmic variation normosmic idiopathic hypogonadotropic hypogonadism, which represent the most severe aspects of the disorder (10,11). Additionally, mirror movements can also be seen. It's a rare genetic disorder that occurs in 1 in 8,000 in men and 1 in 40,000 in women (3,8,9). This syndrome also affects the olfactory system. This predicts that the development of other axonal pathways may also be affected, thus causing damage to the axonal pathways in the motor system. In cranial MRI, especially in coronal sections, the olfactory bulb may not be visible (3). The olfactory bulbus was prominent in the cranial MRI in our case. Anosmia/hiposmia was not present. In functional MRI, it was seen that cortical motor areas were activated in the contralateral of the both the hand that actively moved and the hand that contracted involuntarily.

In many studies studied on mirror movements, it has been shown that voluntary one-sided hand movement leads to bilateral motor cortex activation. Positron emission tomography, electroencephalography and simultaneous EMG, transcranial magnetic stimulation and functional MRI have been used in some studies to demonstrate this (3,10). Diffusion tensor imaging or functional MRI has recently come to the fore as neuroimaging to evaluate mirror movements. Changes in the corpus callosum volume, reduction in transcallosal motor fibers, and bilateral motor cortex activation can be seen in functional MRIs (1). We also think that when such complaints are encountered, functional MRI should primarily be kept in mind and preferred to show the etiopathology non-invasively, in a better and shorter time and to assist in the distinction between acquired and congenital forms.

Ethics

Informed Consent: Consent has been taken.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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Video 1.

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