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Individuals with a COVID-19 history exhibit asymmetric gait patterns despite full recovery

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A B S T R A C T

COVID-19 is a multisystem infectious disease affecting the body systems. Its neurologic complications include -but are not limited to headache, loss of smell, encephalitis, and cerebrovascular accidents. Even though gait analysis is an objective measure of the neuro-motor system and may provide significant information about the pathophysiology of specific diseases, no studies have investigated the gait characteristics in adults after full recovery from COVID-19. This was a cross-sectional, controlled study that included 12 individuals (mean age, 23.0 ± 4.1 years) with mild-to-moderate COVID-19 history (COVD) and 20 sedentary controls (CONT; mean age, 24.0 ± 3.6 years). Gait was evaluated using inertial sensors on a motorized treadmill. Spatial-temporal gait parameters and gait symmetry were calculated by using at least 512 consecutive steps for each participant. The effect-size analyses were utilized to interpret the impact of the results. Spatial-temporal gait characteristics were comparable between the two groups. The COVD group showed more asymmetrical gait patterns than the CONT group in the double support duration symmetry ($p = 0.042$), single support duration symmetry ($p = 0.006$), loading response duration symmetry ($p = 0.042$), and pre-swing duration symmetry ($p = 0.018$). The effect size analyses of the differences showed large effects ($d = 0.68$–0.831). Individuals with a history of mild-to-moderate COVID-19 showed more asymmetrical gait patterns than individuals without a disease history. Regardless of its severity, the multifaceted long-term effects of COVID-19 need to be examined and the scope of clinical follow-up should be detailed.

1. Introduction

COVID-19 is a complex disease affecting many organ systems and physiological processes. Although it is primarily a respiratory tract and lung infection, COVID-19 can involve the central nervous system and lead to neurologic symptoms and disorders as well. Current data reveal that neurological manifestations of COVID-19 including encephalitis, seizures, necrotizing encephalopathy, and cerebrovascular accidents may lead to incapacitating sequelae or long-term symptoms known as long-haul COVID or long COVID (Balcom et al., 2021; Crook et al., 2021; Nersesjan et al., 2021). CDC states that "it is a range of symptoms that can last weeks or months…[that] can happen to anyone who has had COVID-19" and there are no accepted diagnostic criteria (Phillips and Williams, 2021). The most commonly reported symptom of long COVID is fatigue followed by poor memory, concentration deficits, sleep disturbances, and 'brain fog' (Crook et al., 2021). Although there were several studies on the physical findings of individuals after COVID-19, it has been observed that these studies were mostly conducted on individuals with severe symptoms. Studies on the long-term effects of mild to moderate forms of the COVID-19 virus, whose mode of action has not yet been fully clarified, are still limited (Carvalho-Schneider et al., 2021; Clauw et al., 2020; Havervall et al., 2021). Musculoskeletal impairments after severe COVID-19 were also recorded as fatigue, myalgia, and arthralgia (Godaert et al., 2020; Pung et al., 2020) and long-COVID symptoms can be reached for 3–6 months (Abdullahi et al., 2020; Cipollaro et al., 2020; Karaarslan et al., 2022; Malik, 2022). Musculoskeletal symptoms are usually attributed to indirect effects resulting from inflammatory and/or immune responses, but it is assumed that there may be other mechanisms, such as direct damage of the virus on the endothelium or peripheral nerves (Cipollaro et al., 2020). It is

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possible that these symptoms, observed in the long term after severe cases of COVID-19 with lung involvement, affect gait. However, it was observed that there were no studies on the gait of individuals who had a history of mild to moderate COVID-19 who had fully recovered from COVID-19, and who did not have symptoms after COVID-19.

Gait is an important routine function and is the final output of a person's neuromotor control system (Hausdorff, 2005) and is a skill that provides good information about the interplay of the individual's musculoskeletal system with other internal systems (Hausdorff, 2005). It has been reported that many neurological damages that could occur after COVID-19 may affect gait by impairing cerebellar coordination (Helms et al., 2020). In a study, the researchers examined the neurological effects of individuals with and without typical COVID-19 symptoms. They stated that neurological symptoms could be observed in both COVID-19 groups (Chuang et al., 2021). However, except for some cases, gait-related findings in fully recovered individuals have not been studied. In a study, an ataxic gait was detected in an individual who had lung involvement due to COVID-19, although all laboratory and imaging tests, including central nervous system functions, were normal during the recovery period. The authors, who did not determine the reason for this, only reported the gait disturbance observed despite improvement (Dijkstra et al., 2020). Also, there was a case report on a pediatric case of post-COVID-19 acute disseminated encephalomyelitis presented by complaints of right upper extremity paresis, truncal ataxia, and gait disturbance (McLendon et al., 2021). It has been reported in another study that coordination and gait disturbance was detected after COVID-19 in another individual who did not have any neurological disease in the past (Pistoia et al., 2021). Although the organic factor has not been fully revealed yet, there are such studies expressing disruption in the neural system-related gait functions after COVID-19. Therefore, it has been thought that it could be important to examine gait, an important function of the neural system, after full recovery from COVID-19. Also, there was no comparative study that investigated the gait characteristics in adult post-COVID-19 individuals after full recovery. Hence, the current study was planned as the first part of a comprehensive project to examine the gait characteristics of adult volunteers who had a history of mild-to-moderate COVID-19 and were apparently healthy.

Our hypothesis was based on the idea that individuals with and without a history of COVID-19 may exhibit different gait parameters.

2. Material and methods

2.1. Participants

Volunteers were recruited for the study by hand brochures, social media announcements, and posters. Inclusion criteria were COVID-19 history without hospitalization at least two months ago, mild-to-moderate symptoms based on the current classification, medical treatment prescribed according to guidelines, no vaccination before the disease, and sedentary lifestyle. The control group was comprised of sedentary peers without vaccination and any chronic disease history. Exclusion criteria for both study and control groups were the presence of any chronic disease, history of fall, trauma, or surgery in the last year, using alcohol, painkillers, or recreational drugs in the last 48 h, any medication during research, chronic pain, the history of COVID-19 more than once.

2.2. Treatment of COVID-19 during the data collection period in TURKEY

At the time of the study, COVID-19 treatment in patients with mild and moderate symptoms in Turkey was administered with hydroxychloroquine, favipiravir, remdesivir, tocilizumab, anakinra, paracetamol, and vitamin C. Different treatments were used for patients with a severe course or patients with signs of lung involvement (İnkaya et al., 2020; Yavuz and Ünal, 2020; Yeşil et al., 2021). All participants with mild to moderate COVID-19 history in our study had used a treatment containing hydroxychloroquine, favipiravir, paracetamol, and vitamin C.

2.3. Diagnosing process of COVID-19 in Turkey

The diagnosis of COVID-19 is made by RT-PCR (Realtime Reverse-Transcriptase Polymerase Chain Reaction) test from secretion samples taken from the upper or lower respiratory tracts. Chest computed tomography (thorax CT) is performed for individuals who had negative RT-PCR tests and had additional findings of respiratory system involvement. In cases where bilateral, multiple, usually peripheral-subpleural localized, focal ground-glass opacities and sometimes consolidated areas are seen as a result of CT, COVID-19 treatment is initiated.

The national health record base (https://enabiz.gov.tr/) of Turkey includes individuals' entire health history (tests, treatments, etc.). Participants were asked to create and bring a report from the tab which contains information about their COVID-19 history (my COVID-19 status) and information about whether they have chronic diseases and their recent treatments. This system is a network where the personal data protection system is kept at a high level, which can be accessed by the person and the health care team who intervenes in the person in a condition of the individual's permission. The authenticity of the report can be verified using the data matrix in the reports brought by the individuals and the HES codes of the individuals. HES codes are created individually, with this code, COVID-19 stories, and current COVID-19 risk situations can be questioned.

Our participants were requested to bring a Ministry of Health-approved document regarding their e-Pulse (the national health record base system) COVID-19 status. Accordingly, individuals with COVID-19 who were diagnosed with RT-PCR test followed up with standard treatment protocol, and whose treatment was terminated with a negative RT-PCR test, without a history of lung involvement, were included. These individuals also documented that they were not yet vaccinated, nor were they infected with the variant, with e-Pulse documents containing their vaccination history.

In addition, the same documents were also requested from the control group. Participants who fully met the inclusion criteria were included in the study.

2.4. Classification of the symptoms of COVID-19 disease

Although the definitions of the severity of COVID-19 have not yet been clarified, classification is generally used clinically such as the following in common (İnkaya et al., 2020; Yavuz and Ünal, 2020; Yeşil et al., 2021).:

- Asymptomatic: The positive RT-PCR test without any symptoms.
- Mild COVID-19: A mild cold, runny nose, mild fever, pain, and etc. symptoms.
- Moderate COVID-19: A fever accompanied by musculoskeletal signs such as significant pain and fatigue.
- Severe COVID-19: The symptoms with signs of lung involvement and positive CT results.

We included individuals with mild to moderate symptoms who received the appropriate standard treatment and had a negative test result on the 14th day of their disease (routine practice in Turkey) with complete recovery from symptoms. The control group consisted of those without a history of COVID-19.

2.5. Questioning the sedentary lifestyle

According to the guidelines of the American Dietetic Association and the American College of Sports Medicine (ACSM); an active individual should do moderate-intensity physical activity for at least 30 min every day or most days of the week (https://www.acsm.org/). Individuals with a physical activity level below this are considered sedentary individuals. In our study, the physical activity level of individuals according to this definition was questioned and individuals who led a sedentary life were included in the study.

Thirty-six individuals were screened for suitability and four individuals were excluded (flow diagram). The final analysis included 12 individuals with a history of COVID-19 (COVD; M/F = 6/4; mean age, 23.0 ± 4.1 years), and 20 controls (CONT; M/F = 7/13; mean age, 24.0 ± 3.6 years).

Time after COVID-19 was calculated as the number of days from day 14 when each individual's RT-PRC test came back negative.

2.6. Gait analyses

First of all, the participant's preferred speed was determined on the motorized treadmill (Hinton et al., 2018) and a 4–5 min familiarization period was applied to the treadmill at this speed. Then, a resting period followed. After the resting period ended, the inertial sensors were positioned on appropriate anatomical landmarks of participants (MTw, Xsens Technologies BV, Enschede, The Netherlands) which were placed on the dorsum of both feet, tibia crests, lateral sides of femur, sacrum, and proximal sternum (Steins et al., 2014; TarniŢă, 2016). Anthropometric data (body height, foot length, shoulder height, shoulder width, elbow span, arm span, wrist span, hip height, hip width, knee height, ankle height) were entered into the system, and an animation of each individual was created together with standard calibration before proceeding to gait analysis. The gait parameters were normalized according to the anthropometric characteristics of the person. The calibration at the beginning of the gait analysis was therefore performed and repeated before each individual. Gait analyzes were performed barefoot. Participants walked using masks due to COVID-19 precautions. Then, the individual was included in the gait analysis at his/her determined gait speed.

At least 512 steps were collected from each individual for the accuracy of the analysis. Spatial and temporal gait data were collected, and their inter-step differences were recorded to assess gait symmetry. Inter-step differences were calculated separately for each step parameter, and the mean and standard deviations were determined over the differences in their consecutive data. Evaluations were performed by the same researcher who was blinded to the individuals' COVID-19 history.

2.7. Statistical analyses

Descriptive data were presented as means and standard deviations. Normality of variates was tested by Kolmogorov-Smirnov test. Intergroup comparisons were performed by the Mann-Whitney *U* test. The effect size analysis was performed to examine the minimal clinically important difference of the results in cases where differences were observed. The Cohen d intervals were used for the effect size classification: the low effect (d = 0.20), the medium effect (d = 0.21–0.5), and the large effect (d = 0.51–1.0). The power of the study was calculated using the program GPower 3.0.10 (Universität Kiel, Germany). The pre-swing duration symmetry was used to calculate the power of the study. The power of the study with an effect size of 0.831with 32 participants was determined as 80%. The statistical significance level was set to $p < 0.05$.

The process of the study was summarized in Fig. 1.

3. Results

The general characteristics of the groups were given in Table 1. The COVD and the CONT groups were comparable in terms of mean age, height, BMI, and preferred gait speed ($p > 0.05$). In the COVD group, the time elapsed after recovery was 58 ± 23.6 days. The gait parameters in the two groups were presented as spatial-temporal and symmetry. Spatial-temporal gait parameters were given in Table 2. Spatial and temporal gait parameters of both sides (left and right) were similar in the COVD and CONT groups. Also, there was no difference between the

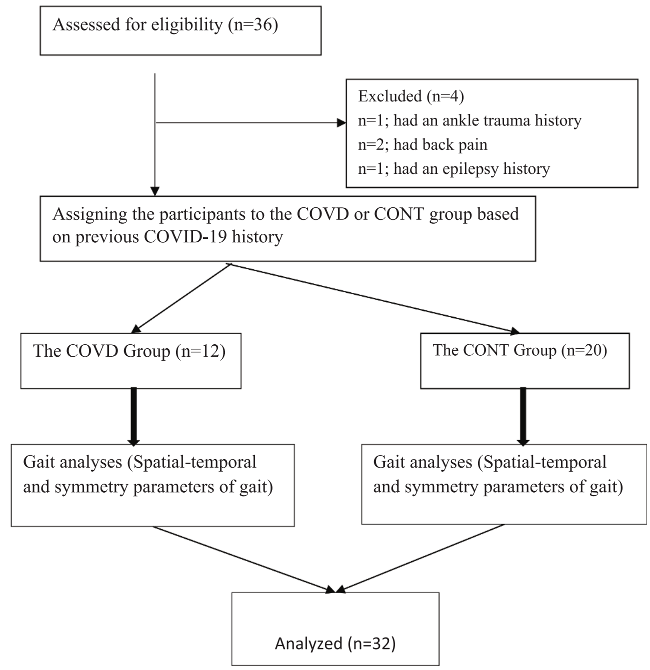

Fig. 1. Flow Diagram of the Study.

Table 1
General characteristics of the study groups.

	COVID group N = 12	Control group N = 20	P value
Age, year	23.0 ± 4.1	24.0 ± 3.6	0.693
Height, m	1.70 ± 0.16	1.68 ± 0.17	0.218
BMI, kg/m2	23.0 ± 3.4	22.8 ± 3.5	0.195
Time after COVID-19, day	58 ± 23	–	

Abbreviations: BMI, body mass index.

Table 2
Comparison of spatial-temporal gait parameters.

	COVID group N = 12	Control group N = 20	P value
Gait speed, m/sec	0.69 ± 0.10	0.77 ± 0.18	0.116
Left			
Step length, cm	45.6 ± 8.5	46.4 ± 11.3	0.612
Step width, cm	9.8 ± 3.7	9.5 ± 4.2	0.353
Stride length, cm	91.7 ± 15.1	94.5 ± 20.4	0.554
Single support duration, sec	0.50 ± 0.05	0.48 ± 0.04	0.687
Double support duration, sec	0.13 ± 0.02	0.12 ± 0.02	0.822
Loading response duration, sec	0.13 ± 0.02	0.12 ± 0.02	0.317
Mid-stance duration, sec	0.24 ± 0.02	0.23 ± 0.02	0.453
Terminal stance duration, sec	0.26 ± 0.03	0.24 ± 0.05	0.799
Pre-swing duration, sec	0.14 ± 0.02	0.12 ± 0.03	0.126
Right			
Step length, cm	46.1 ± 7.0	48.0 ± 9.7	0.612
Step width, cm	9.8 ± 3.7	9.5 ± 4.2	0.353
Stride length, cm	91.7 ± 15.1	94.5 ± 20.4	0.554
Single support duration, sec	0.51 ± 0.05	0.48 ± 0.04	0.261
Double support duration, sec	0.14 ± 0.02	0.12 ± 0.03	0.229
Loading response duration, sec	0.14 ± 0.02	0.12 ± 0.03	0.126
Mid-stance duration, sec	0.23 ± 0.03	0.23 ± 0.03	0.287
Terminal stance duration, sec	0.28 ± 0.05	0.24 ± 0.04	0.309
Pre-swing duration, sec	0.13 ± 0.02	0.12 ± 0.02	0.317

groups in the spatial parameters of the gait symmetry. On the other hand, temporal parameters of the gait symmetry were significantly different in the COVD group (Table 3). Double and single support symmetry, loading response duration symmetry, and pre-swing duration symmetry measurements revealed that the COVD group had more asymmetrical gait patterns than the CONT group in the temporal parameters of gait. Statistical analyses showed that the Cohen-d effect size of the double support duration symmetry (d = 0.736), the single support duration symmetry (d = 0.68), the loading response duration symmetry (p = 0.756), the pre-swing duration symmetry (p = 0.831) were statistically significant. All different values showed large effects.

The results of the study were summarized in Tables 1-3.

4. Discussion

The results of the study showed that sedentary individuals with a mild to moderate history of COVID-19 exhibited more asymmetrically than individuals without a history of COVID-19.

Recently, using the inertial measurement units (IMUs) to examine the outcomes or clinical conditions of any individual, has been increasing preferably (Routhier et al., 2020). IMUs are lightweight, allow 3D motion analysis, and are preferred in gait analysis because they facilitate independence from physical space (Routhier et al., 2020). IMUs are also considered useful for practically collecting multiple sequential data to measure gait characteristics of gait disorders (Zhao et al., 2017). It has been shown that IMUs were quite successful in detecting the minimally detectable change in many diseases such as Parkinson's, stroke, and cerebral palsy in which gait or any movement was significantly affected (Bhavana et al., 2016; Carmona-Pérez et al., 2020; Felius et al., 2022). In addition, the IMUs were accepted as valid and reliable measurement tools that can detect minimal changes in movements in healthy conditions as well as in diseases. IMUs have distinct advantages over many cross-sectional data collection methods in the sequential data collection process and provide the user with a convenient opportunity to study or train ongoing motion (Marín et al., 2020; Persson, 2018; Washabaugh et al., 2017). For these reasons and because our participants were individuals who were considered healthy, we preferred to use IMUs in our research. Thus, we collected our data with a method sensitive to small changes.

Previous studies implied that examining the time series in gait analysis was useful to optimally reflect the neurophysiological nature and real characteristics of gait and also emphasized that it could be an optimal method to collect at least 512 consecutive data from the studied series to achieve the goal (Alcan, 2021; Crevecoeur et al., 2010; Phinyomark et al., 2020). Since the present study was a step of a large-scale project, we tried to make our results relatively more precise by collecting the time series in optimal conditions. We preferred the 512 consecutive steps method in our study. However, different researchers may adopt different valid methods.

For gait symmetry, both the neuromotor organization should be optimal and the musculoskeletal system should not be affected by an asymmetrical pathology (da Cunha-Filho et al., 2003; Viteckova et al., 2018). Even in healthy individuals, gait asymmetry can be observed, but there is no definite judgment in the literature regarding the ideal degree of this. However, studies showed that as asymmetry in gait increased, energy consumption increased, quality of life decreased, and bone mineral density was affected. (Lord et al., 2013; Sadeghi et al., 2000; Verghese et al., 2007). Along with these, symmetrical gait, which is an important output of neural control, is one of the measurements that can determine cognitive decline and fall risk (Beauchet et al., 2009). It has been shown that evaluations of gait symmetry are sensitive in distinguishing between healthy gait and gait disorders. It has also been reported that the greater the problem causing the pathological gait, the greater the asymmetry of the gait (da Cunha-Filho et al., 2003; Viteckova et al., 2018).

In the literature, asymmetric gait is often attributed to neurological or cognitive problems (da Cunha-Filho et al., 2003; Viteckova et al., 2018). Individuals without peripheral musculoskeletal involvement should be able to multitask, be cognitively alert, and have good psychological health to exhibit symmetrical gait (Kikkert et al., 2017; Yogev et al., 2007). In our study, our participants did not have ongoing symptoms, however, those with a history of COVID-19 had asymmetry in their gait compared to the control group. In previous reports in the literature, it has been reported that gait disturbances were observed even after full recovery in people who had COVID-19 with pulmonary involvement. It has been reported that a case showed ataxic gait resembling the finding of cerebellar involvement, although they did not have central nervous system damage (Dijkstra et al., 2020; Pistoia et al., 2021). Also, coordinated gait is related to the central nervous system as well as the peripheral nervous system's processing of sensory information. There is research in previous studies reporting that peripheral nerves can be affected by COVID-19 (Cipollaro et al., 2020). Another study reported that some long-term problems were detected in brain structures due to COVID-19 (Douaud et al., 2021). In this study, it was emphasized that there was a thinning in the structure of the gray matter and parahippocampal gyrus, a decrease in global brain size, and deterioration in sensory functional areas associated with the limbic system (Douaud et al., 2021). From a general perspective, it can be said that these structures are the basic structures that take part in the operation required for the symmetry of gait. However, no differential results were reported in this study (Douaud et al., 2021) in terms of the severity of symptoms. In our study, we aimed to examine whether the gait of individuals who had mild-to-moderate COVID-19 was affected. Our question was? Whatever the cause, what if a history of mild to moderate COVID-19 also produces effects that cannot be detected by routine clinical observations? To investigate this research question, we decided to use a long-range gait analysis that would be an effective measure by using inertial sensors.

In our study, we observed that the stride lengths of the participants were relatively short compared to the norms declared in the literature (Liu et al., 2014; Latorre et al., 2019). We thought that the reason for this might be regional differences. Norm studies generally identify useful reference values for a particular group. However, to generalize to the whole population, individuals with different anthropometric structural characteristics from different regions should be included in the sample pool with appropriate statistical ratios. We thought that the difference in our study may be due to this, we did not look for any pathological cause in the aspect of the step lengths. In addition, this may also be due to the Hawthorne effect. Of course, participants may tend to behave differently under observation. However, we thought that this behavior can also be observed in other samples presented in the literature.

There were some limitations of the present study. Although there is no literature support regarding the COVID-19 effects of asymptomatic individuals on their health conditions, the inability to distinguish asymptomatic individuals in the current study was among the limitations. Simultaneous RT-PCR testing could be performed to detect asymptomatic individuals. That would have made the research much more powerful. Moreover; individuals may have experienced COVID-19

Table 3
Comparison of gait symmetry parameters.

	COVID group N = 12	Control group N = 20	P value
Step length, cm	0.487 ± 4.210	1.602 ± 5.151	0.767
Step width, cm	0.022 ± 0.037	0.008 ± 0.032	0.202
Stride length, cm	0.008 ± 0.036	0.003 ± 0.027	0.701
Single support duration, sec	0.015 ± 0.017	0.005 ± 0.013	**0.006**
Double support duration, sec	0.013 ± 0.012	0.004 ± 0.013	**0.042**
Loading response duration, sec	0.013 ± 0.012	0.003 ± 0.014	**0.042**
Mid-stance duration, sec	0.003 ± 0.016	0.004 ± 0.024	0.699
Terminal stance duration, sec	0.017 ± 0.019	0.001 ± 0.023	0.065
Pre-swing duration, sec	0.014 ± 0.011	0.004 ± 0.013	0.018

in the past and have completed this process asymptomatically. But, based on the hypothesis of the present research, this issue was ignored because it was desired to examine the post-COVID-19 results of people who showed mild to moderate symptoms due to COVID-19 and received their treatment. Also, we did not measure the effects of being carried out with a mask the evaluations we used. The use of masks during the research may have reduced the comfort of the participants. Although the results showed that the two groups were different, the results did not provide information about the performance they would perform without the mask, individually. We can consider this as another limitation. However, we interpreted the comparative results of the groups by ignoring the mask. Because all participants used the mask during the evaluation period. When the pandemic is over and the use of masks is no longer a necessity, this type of research can be conducted without a mask. Thus, the effect of mask use on physical performance can be investigated in many ways. We prioritized complying with COVID-19 precautions in our research.

The present study showed that young sedentary individuals with a mild to moderate COVID-19 history had more asymmetrical gait patterns than individuals without COVID-19. It is recommended to examine the factors affecting the symmetry in the gait of individuals after COVID-19 and the gait characteristics of individuals who have had different severity of COVID-19 in future studies.

CRediT authorship contribution statement

Hilal Keklicek: Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Halit Selçuk:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **İlke Kurt:** Writing – review & editing, Editing – original draft, Methodology, Formal analysis, Conceptualization. **Sezer Ulukaya:** Writing – review & editing, Editing – original draft, Methodology, Formal analysis, Conceptualization. **Gülnur Öztürk:** Writing – review & editing, Editing – original draft, Methodology, Formal analysis, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' contributions

I.K. and G.O: Data screening, data collecting, review literature, proofreading. H.K and H.S: conceptualization, data collecting, analysis, interpretation of results, manuscript drafting, and proofreading. S.U.: Data screening, data collecting, review of literature, proofreading

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