ORIGINAL RESEARCH

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Impact of Sleep Quality on Disease Activity and Clinical Outcomes in Older Patients with Inflammatory Bowel Disease

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Abstract

Objective: Sleep quality can affect how inflammatory bowel disease (IBD) is assessed, managed, and monitored in older patients. This study aimed to investigate the relationship between sleep quality, geriatric syndrome, and IBD disease activity in older patients.

Materials and Methods: This study included a cohort of 91 individuals diagnosed with IBD. The Harvey-Bradshaw Index (HBI) and mayo score (MS) were used as tools for assessing disease activity in crohn's disease (CD) and ulcerative colitis (UC), respectively. The Pittsburgh sleep quality index were used (PSQI) to evaluate sleep quality. A logistic regression analysis was performed to identify the independent components of sleep quality.

Results: The median age of the patients was 60 (50-80) years, and 44% (n=40) of the patients were female. The CD group accounted for 46.2% (n=42) of the IBD group. Sleep quality was impaired in 47.6% (n=20) in CD and 46.9% (n=23) in UC. The HBI of those with poor sleep quality was statistically higher than that of those with normal sleep quality [5 (2-9) vs. 4 (1-8), p=0.035]. No significant relationship was found between sleep quality and MS. There was a moderately significant correlation between the PSQI score and the HBI (r=0.509, p=0.008); on the contrary, there was no significant correlation between the PSQI score and MS. Those with active CD had a higher PSQI score than inactive disease [score 6 (1-11) vs. 3 (1-7), p=0.005]. Upon logistic regression analysis, the parameters independently related to sleep quality were GDS-15 [OR=1.680 (1.294-2.180), p<0.001], urinary incontinence [OR=7.706 (1.177-50.463), p=0.033], and 4-m gait speed [OR=0.360 (0.002-0.617), p=0.022].

Conclusion: In patients with IBD, sleep quality can be affected not only by disease activation and geriatric syndromes. Therefore, a comprehensive and inclusive approach, including the utilization of comprehensive geriatric assessment, may be an important component of patient management.

Keywords: Sleep quality, inflammatory bowel disease, geriatric assessment, comprehensive geriatric assessment, activity score

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Introduction

Inflammatory bowel disease (IBD) is a chronic illness that presents with various symptoms, including abdominal pain, unintended weight loss, diarrhea (with or without hematochezia), developmental delays, pyrexia, dermatological manifestations, sporadic arthralgia, and joint effusion. IBD frequently presents as two distinct conditions known as ulcerative colitis (UC) and Crohn's disease (CD). Therapy for inflammatory bowel illnesses poses various obstacles, including the chronicity of the condition, influence of patient tiredness on quality of life, potentially severe adverse effects of drugs, and occasional treatment resistance (1).

Sleep disturbances are commonly reported in patients with chronic inflammatory illnesses and are acknowledged as a significant contributing factor to worsening their condition (2). Assessing sleep disruption in patients with IBD is essential, regardless of disease stage. Poor sleep quality may indicate subclinical inflammation, which is a valuable indicator for disease monitoring and treatment. Therefore, it is crucial to incorporate sleep quality assessment into the diagnostic process of IBD (3,4). Sleep disturbances are commonly examined using subjective scales in research studies. The Pittsburgh Sleep Quality Index (PSQI) is commonly used as a metric in cases of IBD (5).

Multiple factors contribute to the onset of sleep disruption among patients diagnosed with IBD. Several factors can influence an individual's sleep quality, such as sadness and anxiety, the presence of an active disease, advanced age, cognitive functioning, elevated levels of inflammatory markers, and substance abuse (6). The application of comprehensive geriatric assessment (CGA) is essential for identifying and managing the diverse psychological, physical, and cognitive challenges frequently observed in the elderly population (7). The sleep quality of older adults diagnosed with IBD is impacted by a range of factors, with geriatric syndromes playing a notable role, particularly in IBD activity.

The primary aim of this research endeavor is to investigate the potential association between sleep quality and clinical outcomes, namely the manifestation of IBD disease and geriatric syndromes, among patients aged 50 years or older who are diagnosed with IBD.

Materials and Methods

Study Design

The research was approved by the Assessment and Evaluation Ethics Sub-Working Group of Hacettepe University Ethics Committee (approval number: 2019/28-29, date: 03.12.2019). Verbal and written informed consent was obtained from all patients.

The present investigation was carried out at the outpatient clinics of Geriatric Medicine and Gastroenterology, situated within a university hospital, from December 4, 2019 to December 4, 2020. This study included individuals aged 50 years who were diagnosed with IBD and sought care at a gastroenterology outpatient clinic for six months. The individuals in question were directed to the geriatric medicine outpatient clinic to undergo comprehensive geriatric assessment and have their sleep quality evaluated subsequent to determining their activation scores. Individuals who were excluded from the study were those with unstable general illnesses, psychiatric disorders, and drug use that had the potential to impact sleep. In total, a subset of 101 patients who were recommended for study inclusion were assessed. Among them, three patients were not in a stable condition, five patients declined to participate, and two patients were eliminated from the study due to their use of antihistamine medications, which have the potential to impact sleep. Consequently, the present investigation was undertaken with a sample size of 91 individuals. Sociodemographic information, chronic medical conditions, medication usage, and timing of IBD diagnosis were documented for the study participants. The comorbid diseases of the patients were assessed using the Cumulative Illness Rating Scale-Geriatric (CIRS-G) scale. The CIRS-G was developed to assess the likelihood of survival among elderly individuals. This assessment employs a scoring mechanism that spans 0 to 4 points, denoting the extent of disease severity across 14 distinct organ systems. The scale's total score spans 0-56 points (8). Following that, the patients received a CGA performed by the same geriatrician. The study assessed various measures related to the functioning and well-being of older adults. These measures included the activities of daily living (ADL) (9,10), instrumental activities of daily living (IADL) (11,12). Mini nutritional assessment-short form (MMSE) (13,14). Fifteen-item geriatric depression scale (GDS-15) (GDS-15) (15,16). Mini nutritional assessment-short form (MNA-SF) (17,18), and 4-m gait speed test. Additionally, grip strength, urinary incontinence (UI), and falls were examined as part of the CGA. The PSQI (19,20) was used to evaluate the sleep quality of the participants.

CGA Parameters

The ADL, which stands for ADL, is a comprehensive assessment tool that evaluates an individual's functional abilities in six domains (9). The scale was validated in a Turkish population by Arik et al. (10). The IADL encompasses a comprehensive set of eight areas: shopping, telephone usage, laundry, housekeeping, food preparation, transportation utilization, prescription management, and financial management (11). Turkish validation of IADL was carried out by Isik et al. (12) The MMSE was designed to evaluate the cognitive functioning of individuals (13). Güngen et al. (14) conducted a validation

study on the MMSE for the Turkish population. The GDS-15 is a psychometric instrument with a numerical range ranging from 0 to 15, specifically designed for evaluating the emotional state of elderly individuals; a score of 5 on binary response questions suggests that the patients being surveyed are potentially susceptible to experiencing symptoms of depression (15). Ertan and Eker (16) conducted research to validate the GDS-15 in the Turkish population. The MNA-SF was employed to evaluate the presence of malnutrition and validated in a Turkish population (17,18).

Assessment of Sleep Quality

PSQI is a thorough assessment tool used to measure sleep quality. The survey comprised a comprehensive set of 24 items, where 19 items were self-reported by the patients, and the remaining five items were completed by their cohabiting partners. Although the scoring method does not incorporate the replies supplied by partners, the inputs offer significant insights into the sleep patterns exhibited by the patients.

Seven specific factors were evaluated to calculate the PSQI score, including subjective sleep quality, sleep onset latency, total sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medicine, and daytime impairment. The cumulative index score is obtained by adding the scores of the seven components together. The PSQI score ranges from 0 to 21, with a score of 5 indicating suboptimal sleep quality. A higher composite score indicates an increased prevalence of sleep quality issues (19). Ağargün et al. (20) validated the PSQI of the Turkish population.

IBD Activity Scores

In this study, two activity indices were used to assess the activity level of individuals diagnosed with IBD. The Harvey-Bradshaw Index (HBI) was employed to assess patients diagnosed with CD. The HBI encompasses four distinct categories: general well-being, abdominal pain, frequency of daily bowel movements, and presence of complications. The cumulative score derived from the index ranged from 0 to 26 points. According to a previous study, a score of 5 points indicates remission, whereas a score ranging from 5 to 7 points suggests mild disease.

Additionally, a score ranging from 8 to 16 points is associated with moderate disease, whereas a score exceeding 16 indicates severe disease (21). Remission was determined using an HBI score of 5 points, whereas active disease was defined as a score of 5 points. The study employed the Mayo Score (MS) for UC Activity, which includes four distinct criteria: stool frequency (ranging from 0 to 3), rectal bleeding (ranging from 0 to 3), flexible proctosigmoidoscopy outcome (ranging from 0 to 3), and physician's global assessment (ranging from 0 to 3). The overall score ranged from 0 to 12, with higher scores indicating greater disease activity (22).

Statistics

The IBM Statistical Package for the Social Sciences (SPSS) software version 22.0 for Windows is used to perform the statistical analyses. Many statistical techniques are involved in analyzing the distribution of numerical parameters, such as constructing a histogram, calculating the coefficients of variation, and conducting the Kolmogorov-Smirnov tests. The statistical tests used to compare categorical variables are presented in numerical and percentage format (n, %), including the chi-squared and Fisher exact tests. The Mann-Whitney U test and Student's t-test were used to evaluate differences between groups in relation to the distribution of quantitative data. A Spearman correlation analysis is performed for numerical parameters that do not have a normal distribution. A univariate analysis was conducted to investigate the variables associated with sleep quality. The multivariate analysis included parameters that exhibited a p-value of less than 0.05 to identify factors that had a significant independent association with sleep quality using the backward stepwise model. Statistical significance is indicated by a significance level of less than 0.05.

Table 1. Characteristic features of patients with Crohn's disease and ulcerative colitis

	Crohn's (n=42)	Ulcerative colitis (n=49)	p
Age (years)	62 (51-80)	59 (50-76)	0.089
Gender, female	19 (47.5%)	21 (52.5%)	0.820
Time of diagnosis (months)	57.50 (2-468)	73 (3-310)	0.181
CIRS-G	6 (2-11)	5 (2-13)	0.039
CRP (mg/dL)	0.46 (0.13-17)	0.37 (0.10-7.79)	0.537
Number of drugs	4 (1-12)	3 (1-11)	0.688
Handgrip (kg)	25.80 (11-63.80)	33.90 (9.40-55.30)	0.020
ADL	6 (5–6)	6 (5-6)	0.755
IADL	7 (6–8)	7 (6-8)	0.852
MMSE	29 (26–30)	29 (23-30)	0.785
GDS-15	2 (0–12)	2 (0-12)	0.559
MNA-SF	13 (7–14)	14 (8-4)	0.635
Falls	8 (72.7%)	3 (27.3)	0.053
Urinary incontinence	7 (50%)	7 (50%)	0.779
PSQI score	4 (1–11)	5 (1-12)	0.917

Categorical variables are presented as n (%), and skew distributed continuous variables are presented as median (min-max).
CIRS-G: Cumulative Illness Rating Scale-Geriatric, CRP: C-reactive protein, ADL: Activities of daily living, IADL: Instrumental activities of daily living, MMSE: Mini-mental state examination, GDS-15: Geriatric depression scale, MNA-SF: Mini nutritional assessment-short form, PSQI: Pittsburgh sleep quality index

Results

The median age of the patients was 60 years (50-80). The median duration from the initial diagnosis to IBD diagnosis was 66 (range: 2-468) months. Patients diagnosed with CD comprised 46.2% (n=42) of the total number of patients diagnosed with IBD. Table 1 presents the overall traits and demographic attributes of individuals diagnosed with CD and residing in the UC. Based on the characteristics of the CGA, no statistically significant differences were observed between patients diagnosed with CD and those diagnosed with UC, except for the CIRS-G and Handgrip measures. The study observed that the patients' median PSQI score was 4 points, with a range of 1 to 12. A substantial positive association was observed between the PSQI score and HBI (r=0.509, p=0.008). However, no significant correlation was found between the MS and PSQI score (r=0.041, p=0.773). Table 2 presents the correlation between the quality of sleep and the overall features of the patients. No statistically significant correlation was observed between Mayo and PSQI scores. Patients with CD in remission exhibited lower PSQI scores than those with active illness [PSQI score of 3 (1-7) vs. 6 (1-11), p=0.005, respectively]. Table 3 presents the association between PSQI scores and CGA parameters. The analysis revealed substantial correlations between the PSQI score and several CGA parameters, including ADL, 4-meter walking speed, MMSE, GDS-15, and MNA-SF scores. In total, 15.4% of the patient population exhibited symptoms of UI, with 85% of these individuals specifically experiencing urge incontinence. Furthermore, a total of 12% of patients experienced at least one fall within the previous year. No statistically significant link was observed between the pharmaceutical interventions employed for the treatment of IBD and the subjective assessment of sleep quality. Table 4 presents the logistic regression analysis, which evaluates the characteristics independently associated with sleep quality. Harwey-Bredshaw index, GDS -15, falls, UI, 4-m gait speed, and CIRS-G were included in the logistic regression analysis. A review of the correlation between the GDS-15 and PSQI suggested that the GDS-15 score was correlated with the PSQI subcategories, including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction (r=0.358, r=373, r=273, r=364, r=451, r=228, r=264; p<0.001, p<0.001, p=0.09, p<0.001, p<0.001, p=0.030, p=0.012, respectively). 4 meter gait speed test was correlated with the subjective sleep quality, sleep duration, and sleep disturbance subcategories of the PSQI (r=-0.216, r=-0.238, r=-0.367; p=0.040, p=0.023, p<0.001, respectively). Although there was no noteworthy

Table 2. Characteristics of patients by sleep quality

	PSQI normal (n=48)	PSQI abnormal (n=43)	p
Age (years)	61 (50-80)	50 (50-73)	0.521
Harvey-Bradshaw score	4 (1-8)	5 (2-9)	0.038
Mayo score	2 (0-9)	3 (0-12)	0.389
CRP (mg/dL)	0.55 (0.13-17)	0.37 (0.10-7.79)	0.377
Time of diagnosis (months)	67.50 (2-324)	61 (3-468)	0.246
Number of drugs	3 (1-11)	4 (1-12)	0.143
CIRS-G	4 (2-9)	6 (2-13)	0.013
4-m gait speed (m/s)	1.08 (0.53-1.88)	0.84 (0.56-1.31)	<0.001
Handgrip (kg)	35.30 (12.20-63.80)	28.30 (9.40-51.50)	0.163
Falls during the last 1 year	2 (18.2%)	9 (81.8)	0.012
Urinary incontinence	2 (14.3%)	12 (85.7%)	0.002
ADL	6 (5-6)	6 (5-6)	0.864
MMSE	29 (25-30)	28 (23-30)	0.070
GDS-15	1 (0-7)	6 (0-12)	0.001
MNA-SF	14 (10-14)	13 (7-14)	0.001
DM	10 (50%)	10 (50%)	0.781
HT	17 (47.2%)	19 (55.2%)	0.393
COPD	9 (81.8%)	2 (18.2%)	0.039
Gender, female	17 (42.5%)	23 (57.5)	0.083
Use of biological agents	15 (45.5)	18 (54.5%)	0.293
Oral steroid use	7 (50%)	7 (50%)	0.823
Oral 5-ASA	30 (50.8)	29 (49.2)	0.622
Methotrexate use	0 (0%)	2 (100%)	0.221
Azathioprine use	15 (55.6%)	12 (44.4%)	0.644
Topical 5-ASA	11 (68.8%)	5 (31.3%)	0.070
Topical steroids	0 (0%)	2 (100%)	0.492

Categorical variables are presented as n (%), and skew distributed continuous variables are presented as median (min-max).
CIRS-G: Cumulative Illness Rating Scale-Geriatric, CRP: C-reactive protein, ADL: Activities of daily living, IADL: Instrumental activities of daily living, MNA-SF: Mini nutritional assessment- short form, DM: Diabetes mellitus, HT: Hypertension, COPD: Chronic obstructive pulmoner disease, 5-ASA: 5-aminosalicylic acid, MS: Mayo score, PSQI: Pittsburgh sleep quality index, MMSE: Mini mental state examination, GDS-15: Geriatric depression scale

Table 3. CGA and correlation with PSQI

	Spearman's rho coefficient (r)	p
ADL	-0.278	p=0.008
MNA-SF	-0.439	p<0.001
GDS-15	0.637	p<0.001
MMSE	-0.263	p=0.012
4-m gait speed (m/s)	-0.255	p=0.013
Handgrip (kg)	-0.138	p=0.191

ADL: Activities of daily living, MMSE: Mini mental state examination, GDS-15: Geriatric depression scale, PSQI: Pittsburgh sleep quality index, CGA: Comprehensive geriatric assessment

Table 4. Logistic regression analysis to determine the independent correlates for sleep quality

Parameters	Odds ratio	95% confidence interval		p
		Lower limit	Upper limit	
GDS-15	1.680	1.294	2.180	<0.001
Urinary incontinence	7.706	1.177	50.463	0.033
4-m gait speed (m/s)	0.360	0.002	0.617	0.022

Harwey-Bredshaw index, Geriatric depression scale-15, falls, urinary incontinence, 4-m gait speed, and CIRS-G were included in the logistic regression analysis. The backward stepwise model was used, and the last model (Step 4) has been presented in this table.
GDS-15: Geriatric depression scale-15

correlation between grip strength and PSQI score, a significant negative correlation was discovered in relation to the sleep latency and sleep disturbance subcategories of the PSQI (r=-0.234, r=-0.320; p=0.025, p=0.002, respectively).

Discussion

The findings of the current investigation elucidated a correlation between disease activity and sleep quality among individuals diagnosed with CD. Furthermore, our study demonstrated an independent correlation between sleep quality and other factors, such as mood, walking speed, and UI, in individuals diagnosed with IBD.

In this study, no significant distinction was observed in terms of sleep quality scores between patients with CD and those with UK. However, HBI was correlated with sleep quality. Conversely, the MS was not correlated with sleep quality. The current investigation yielded results indicating a lack of association between the quality of sleep and activation of UC disease, which is consistent with the existing scholarly literature on the subject matter. According to the cited citation (3,27-29), it can be inferred that there is supporting evidence for the claim. In addition, Gingold-Belfer et al. (23) demonstrated that individuals diagnosed with CD and experiencing heightened disease activation exhibited suboptimal sleep quality. Nevertheless, the quality of sleep remained unaffected in those who did not experience illness activation. A study conducted by Ali et al. (24) demonstrated a potential association between sleep quality and histological inflammatory activity in individuals diagnosed with CD. In contrast to our research, Bazin et al. (25) employed actigraphy, which is a scientifically validated approach for assessing sleep quality. Prospective studies employing objective assessment methods and involving a substantial number of individuals are necessary to enhance our understanding of the causal association between sleep quality and disease activation.

The GDS-15, 4-meter gait speed test, and UI status, which were included in the CGA, were independently associated with sleep quality. Becker et al. (26) discovered a significant correlation between sleep quality and depression in older patients. The findings of the current investigation indicate that the depression score has a negative impact on all subcategories of the PSQI. Individuals diagnosed with IBD have a higher prevalence of bladder overactivity, nocturia, and urge incontinence. This finding can be attributed to shared sensory afferent neurons connecting the distal colon and bladder and an elevated release of brain-induced neurotrophic factors (27). The increasing intensity and frequency of UI have a detrimental impact on sleep quality. The occurrence of nocturnal incontinence and its frequency has the potential to alter an individual's sleep patterns, resulting in compromised sleep quality (28).

Muscle strength and functionality may influence the sleep quality of older people. The study conducted by Rubio-Arias et al. (29) revealed a positive correlation between improvements in sleep quality and increases in both 4-m gait speed and handgrip strength. The present investigation shows a notable association between 4-m gait speed and PSQI score. This finding can be elucidated by the outcomes of Zhang et al., (30) who suggested that the interplay between muscle strength and sleep quality contributes to the relationship between 4-m gait speed and sleep quality.

In contrast to previous studies (30,31), the current study did not find a statistically significant association between grip strength and PSQI score. Upon analyzing the subcategory scores of the PSQI, a significant association was observed between the subcategories of sleep latency, sleep disruption, and grip strength. The absence of a significant correlation between the overall PSQI score and grip strength may be due to several factors. One potential factor contributing to this phenomenon is the limited sample size of the participants. It is imperative to employ reliable measurement techniques, such as dual-energy X-ray absorptiometry, which is considered the gold standard, to better understand the correlation between muscle power and strength and sleep quality (32).

Assessing the extent of dependency in ADL living is a crucial initial characteristic to consider when evaluating older people. The influence of daily activities on sleep quality has been documented in previous studies (33,34). This study found a statistically significant association between the level of dependency on everyday activities and the quality of sleep.

Malnutrition has been shown to have significant adverse effects on the prognosis of patients with IBD (35,36). Malnutrition has been found to have a negative impact on the quality of sleep experienced by individuals, leading to an increased risk

of developing sleep disorders. Consequently, this can adversely affect the overall quality of life of affected patients (37). In accordance with previous research, the findings of this study indicate a positive association between those experiencing suboptimal sleep quality and elevated MNA-SF scores.

The cognitive status of older adults significantly influences the quality of sleep. Gildner et al. (38) found a favorable association between cognitive test scores and sleep quality. The findings revealed a modest association between the MMSE and PSQI scores, which can be attributed to the lack of homogeneity in the participants' cognitive distributions. Indeed, we determined that only 6% of the subjects exhibited compromised cognitive abilities.

Sleep problems in individuals with CD or UC are closely linked to symptoms assessed by the HBI and MS. Frequent defecation and abdominal pain are primary contributors to poor sleep quality, causing nocturnal awakenings and discomfort that can severely disrupt sleep patterns. Addressing these symptoms through effective disease management can significantly improve the sleep and overall quality of life for affected individuals (39,40).

The study's strength rests in its primary examination of the association between CGA and sleep quality in older individuals with IBD. Prospective studies are required to further investigate the impact of CGA on the sleep quality of individuals with IBD. Moreover, further investigation is required to examine the post-treatment condition of patients and determine the impact of improved sleep quality on geriatric aspects, including nutrition and cognitive function, in individuals with IBD.

Study Limitations

The current study has certain limitations. One notable limitation of this study is the requirement for an impartial metric, such as polysomnography, to assess sleep quality. Moreover, extrapolating the results to a more extensive demographic proved to be difficult given the study's cross-sectional design and restricted sample size. One of the most significant limitations of the study is the lack of an assessment of frailty. Frailty is a geriatric syndrome directly related to an individual's performance, regardless of age, and plays a crucial role in disease prognosis and treatment response. In future studies, the use of appropriate frailty scales for clinical assessment, treatment response, and prognosis evaluation in patients with IBD could contribute significantly to the literature. The inadequate number of both active and inactive patients with CD and UC in our study is a significant issue. This affects the generalizability of the findings. Therefore, these numbers of patients did not yield statistically significant results and could not be generalized. In future studies to investigate the relationship between CGA and severity, researchers should consider an adequate number of active and inactive patients.

Another limitation of our study was the lack of evaluation of sleep, stool frequency, and pain. This assessment could not be performed because the subcomponents of the HBI and Mayo scoring were not recorded in the dataset.

Conclusion

Older IBD patients' treatment and management should not only consider disease activation but also geriatric syndromes, including sleep problems. CGA with its multifaceted approach, can play a significant role in the appropriate evaluation, diagnosis, treatment, and follow-up of this vulnerable population. Incorporating CGA alongside disease activation scores in the management of commonly encountered sleep disturbances should be considered as part of an appropriate approach.

Ethics

Ethics Committee Approval: The research was approved by the Assessment and Evaluation Ethics Sub-Working Group of Hacettepe University Ethics Committee (approval number: 2019/28-29, date: 03.12.2019).

Informed Consent: Verbal and written informed consent was obtained from all patients.

Footnotes

Authorship Contributions

Concept: Ç.Ç., T.Ş., M.G., E.P., B.S., M.G.H., B.B.D., Design: Ç.Ç., T.Ş., A.O.B., İ.B., Y.Ö., O.K., M.C., B.B.D., Data Collection or Processing: Ç.Ç., T.Ş., M.G., O.K., M.G.H., M.C., T.K., Analysis or Interpretation: Ç.Ç., A.O.B., M.G., İ.B., E.P., B.S., M.C., T.K., B.B.D., Literature Search: Ç.Ç., A.O.B., E.P., B.S., M.C., T.K., B.B.D., Writing: Ç.Ç., İ.B., O.K., E.P., B.S., B.B.D.

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