



FACTORS AFFECTING DISEASE ACCEPTANCE IN INDIVIDUALS WITH STROKE: A DESCRIPTIVE STUDY

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Abstract: Acceptance of their illness by individuals who have experienced a stroke is critically important for supporting medication adherence, preventing secondary strokes, and improving overall quality of life. This study aims to identify the factors affecting acceptance of illness in individuals with stroke. In this descriptive study, acceptance of illness (Acceptance of Illness Scale), treatment adherence (Medication Adherence Report Scale), and medication beliefs (Beliefs about Medicines Questionnaire-BMQ-T) were evaluated in 254 ischemic stroke patients (95 women, 159 men; Age: 59.40±15.03 years; Stroke duration: 14.16±20.34 months) between December 2022 and March 2024. The acceptance of stroke patients' illness score was 20.29±6.35 (moderate level), while the treatment adherence score was 23.33±2.47 (good). As acceptance of illness increased, medication adherence also improved ($\rho=0.210$, $P=0.012$). The BMQ-T subscales of Specific Necessity ($\beta=-0.222$, $P=0.000$) and General Overuse ($\beta=-0.225$, $P=0.000$) were identified as independent predictors of acceptance of illness scores. This study found that patients who believe medications are necessary for treatment but also overused exhibit lower levels of illness acceptance. When dealing with illnesses such as stroke, patients' beliefs about medications should not be overlooked when evaluating their acceptance of illness. Revealed that patients who believe medications are necessary for treatment but also overused exhibit lower levels of illness acceptance.


Keywords: Stroke, Acceptance of illness, Medication beliefs, Medication adherence, Nursing


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1. Introduction

Stroke is a serious health problem characterized by focal cerebral function loss resulting from the obstruction of cerebral blood flow due to vascular causes, lasting for more than 24 hours and leading to death worldwide (Coupland et al., 2017). Approximately 17 million people suffer from stroke each year, with 6 million dying as a result of stroke (Virani et al., 2021). Stroke ranks second among causes of death globally and third in the combination of death and disability. Over the past 20 years, the risk of stroke has increased by 50%, and currently, one in every four individuals is at risk of experiencing a stroke (Feigin et al., 2022). The rate of recurrent stroke within five years for individuals with a history of stroke is about 30-43%, with mortality rates increasing further in cases of recurrence (Feng et al., 2010; Jamison et al., 2017; Ruksakulpiwat et al., 2020). To reduce this high risk of recurrence, controlling risk factors and adhering to medication treatment as recommended by physicians are critically important (Virani et al., 2021).

Despite its importance in preventing secondary strokes, adherence to treatment among stroke survivors varies widely, ranging from 33% to 87% (Kronish et al., 2013; Sjölander et al., 2013; Ruksakulpiwat et al., 2020; Zhang et al., 2021; Arkan et al., 2022). Especially in the early stages of stroke, adherence rates are reported to be high and decrease over time (Bushnell et al., 2011; Oliveira-Kumakura et al., 2019; Arkan et al., 2022). Treatment non-adherence can often be unintentional (such as patients forgetting to take medication or being unable to afford medication), but intentional non-adherence based on personal beliefs about the illness, perceived treatment needs, or potential risks is also common (Sjölander et al., 2013). Factors leading to intentional non-adherence are often linked to individuals' belief about their illness and medications (Unni and Shiyanbola, 2016; Ruksakulpiwat et al., 2020).

Acceptance of illness is a process requiring individuals to cope with changes and limitations in their lives, adhere to prescribed treatments, and make lifestyle adjustments to ensure control over their illness (Simmons et al., 2007; Kucukarslan, 2012; Fedorowicz et al., 2021). Many stroke



survivors struggle to accept especially the sudden onset of new disabilities in adapting to daily life (Kowalska et al., 2019; Guzek and Kowalska, 2020). Research indicates that higher levels of illness acceptance positively influence rehabilitation and recovery outcomes (Kurpas et al., 2013; Kapela et al., 2017; Gawor et al., 2021). Studies examining illness acceptance in stroke patients are limited. In the early stages of stroke (2–8 weeks), individuals aged 50 and above exhibit moderate levels of illness acceptance (Guzek and Kowalska, 2020). It has been reported that illness acceptance varies at different levels in various studies, and factors such as increasing age, increasing severity and duration of stroke, deterioration of functional status, low educational level, inability to be occupationally active, polypharmacy, and comorbidities negatively affect illness acceptance (Kowalska et al., 2019; Guzek and Kowalska, 2020; Gawor et al., 2021).

The limited research on illness acceptance and the factors influencing it in stroke patients, along with inconsistent findings in the literature, prompted us to conduct this study (Groeneveld et al., 2019; Guzek and Kowalska, 2020; Ruksakulpiwat et al., 2020). Determining the levels of illness acceptance and the influencing factors among stroke patients can contribute to improving treatment adherence and enhancing the effectiveness of rehabilitation strategies.

The aim of this study is to determine the factors influencing the acceptance of illness among stroke survivors. Research Questions:

- What is the level of illness acceptance among individuals with stroke?
- What are the factors influencing illness acceptance among individuals with stroke?

2. Materials and Methods

2.1. Study Design, Sample, and Setting

This research, conducted to identify the factors influencing illness acceptance among stroke survivors, is a descriptive study. The study was conducted between December 2022 and March 2024 at the Stroke Clinics of Ankara City Hospital (Physical Therapy and Rehabilitation Hospital). Throughout the research period, adherence to the Helsinki Declaration was ensured. Prior to assessment, all participants were verbally and in writing informed about the study, and written consent was obtained from each participant.

Inclusion criteria: (a) Patients having clinical features and radiological evidence of ischaemic stroke, (b) aged 18 years and above, (c) ability to speak, read, and write in Turkish, (d) willingness to participate in the study, (e) Standardized Mini Mental Test score of 24 or above (Figure 1).

Exclusion criteria: (i) Diagnosis of significant psychiatric illness, (ii) presence of a different neurological problem such as brain tumor, hemorrhagic stroke, or head trauma, (iii) concurrent life-threatening illness or clinical

instability, and (iv) inability to complete the questionnaire in its entirety.

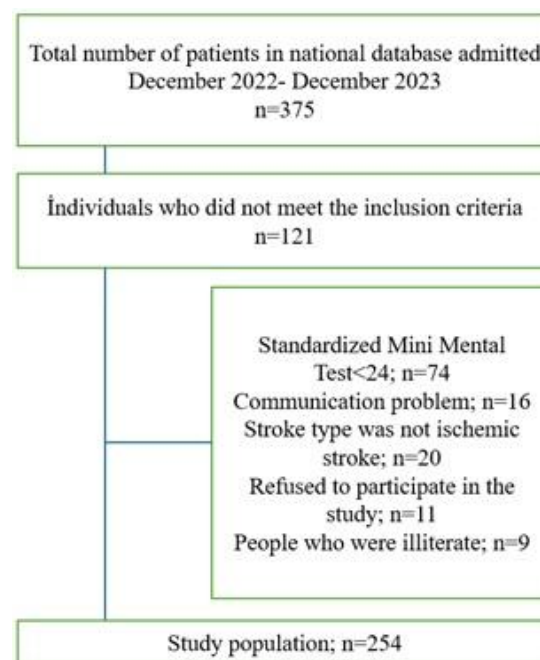


Figure 1. Flow diagram.

2.2. Study Population

The sample size of the study was determined based on correlation coefficients obtained from a similar study conducted by Ruksakulpiwat et al. (2020). Based on a small effect size ($d=0.25$), 95% power, and a statistical significance of $P<0.05$, we calculated a sample size of 254 stroke survivors. G*Power (Version 3.1.9.7, University of Düsseldorf, Düsseldorf, Germany). In this context, a total of 375 stroke survivors were evaluated, of whom 121 did not meet the inclusion criteria (74 individuals had MMSE <24, 16 individuals had communication problems, 20 individuals had a stroke type other than ischemic stroke, 11 individuals refused to participate in the study, and 9 individuals were illiterate), resulting in the inclusion of 254 stroke survivors in the study.

2.3. Data Collection and Procedure

Assessments of participants who consented to participate in the study were conducted during face-to-face interviews by an expert physiotherapist with 10 years of experience in the field. The interviews lasted approximately 15-20 minutes. During the interviews, data were collected using the Data Collection Form developed by the researchers through a review of relevant literature (Bushnell et al., 2011; Jamison et al., 2017; Guzek and Kowalska, 2020; Ruksakulpiwat et al., 2020), the Acceptance of Illness Scale (Besen and Esen, 2011), the Medication Adherence Self Report Scale (Temeloğlu Şen et al., 2019) and the Beliefs About Medicine Questionnaire (Cinar et al., 2016).

Demographic and clinical characteristics: This form includes questions about participants' sociodemographic characteristics (age, gender, marital status, education

level, employment status, smoking status), chronic illnesses, and stroke duration.

Standardized Mini Mental Test (MMSE), a valid and reliable test, individuals scoring 24 points or higher out of a total of 30 points on this scale are reported to have normal cognitive function (Folstein et al., 1975). This test, commonly used in assessing cognitive impairments, evaluates verbal responses involving attention, orientation, and memory, as well as the ability to follow verbal and written commands, spontaneously write sentences, and replicate a complex drawing (Güngen et al., 2002).

Acceptance of Illness Scale (AIS), a valid and reliable scale, assigns a score of 5 to indicate a high level of illness acceptance, while a score of 1 signifies inadequate acceptance of the illness and the presence of negative adaptation. The sixth item in the scale is reverse-coded. Total scores on the scale range from 8 to 40. A high score obtained from the scale suggests a high level of illness acceptance, indicating fewer negative emotions and behaviors associated with the disease (Besen and Esen, 2011). The scale comprises eight questions in a five-point Likert type format, explaining the consequences of health status regarding limitations caused by the disease, deficits in self-sufficiency, feelings of dependency on others, and diminished self-esteem (Felton and Revenson, 1984). Studies utilizing this scale in the literature have interpreted scores between 8-20 as low-level acceptance, 20-30 as moderate-level acceptance, and scores above 30 as high-level acceptance of the illness (Kurpas et al., 2013; Guzek and Kowalska, 2020; Pluta et al., 2020; Fedorowicz et al., 2021).

Medication Adherence Self Report Scale (MARS), which has undergone Turkish adaptation, consists of five questions in a five-point Likert-type format, evaluating medication non-adherence (deciding to skip medication doses, forgetting to take medication, changing medication doses, temporarily stopping medication intake, and taking less than the prescribed dose). Scores obtained from the scale range from 5 to 25. An increase in scores indicates adherence, while a decrease indicates non-adherence (Temeloğlu Şen et al., 2019). It was used to assess adherence to ischemic stroke medications. In previous studies in the literature, a cutoff point of 20 points or higher was considered for adherence. Therefore, we used 20 as the cutoff point in our study (a MARS score <20 was defined as non-adherence) (Sjölander et al., 2013; Ruksakulpiwat et al., 2020; Arkan et al., 2022).

Beliefs About Medicine Questionnaire (BMQ-T), a valid and reliable scale, measures how individuals conceptually evaluate their prescribed medications. The scale consists of two parts evaluating patients' beliefs about the medications they use (specific) and their beliefs about medications in general (general). The specific section consists of two subscales, each comprising five items. The Specific Necessity subscale assesses patients' views on the necessity of their

medications, while the Specific Concern subscale encompasses patients' beliefs about the potential harm and side effects of their medications. Scores obtained from the subscales range from 5 to 25, with item score averages calculated by dividing the subscale scores by the number of questions in each subscale. A high score in the Necessity subscale indicates that patients perceive their medications as important for themselves, while a high score in the Concern subscale indicates that patients have concerns about their medications. The "General" section of the scale consists of two subscales, each comprising four items. The General Overuse subscale evaluates how patients perceive the scope of medication use, while the General Harm subscale indicates patients' general beliefs about the harmful nature of medications. Total scores obtained from these subscales range from 4 to 20, with item score averages calculated by dividing the total subscale scores by the number of questions in each subscale. A high score in each subscale indicates a generally negative perception of medications (Cinar et al., 2016).

2.4. Statistical Analyses

The data analysis of the research results was conducted using the SPSS (Statistical Package for Social Sciences) 27.0 software package in a computer environment. Descriptive variables were expressed as mean \pm standard deviation or median (Interquartile Range (Q1-Q3)), while categorical variables were expressed as numbers and percentages. The Kolmogorov-Smirnov test was used to test the normality of the data. Mann-Whitney U Test was used for comparisons between two groups, and the Kruskal-Wallis test was used for comparisons among more than two groups. Bonferroni correction was used for pairwise comparisons among multiple groups. Since the data is not normally distributed, a Spearman correlation analysis was conducted to determine the correlation between the variables (Önder, 2018). Multiple linear regression analysis (Kurnaz et al., 2021) was conducted to identify the most influential variables affecting illness acceptance. Statistical significance was set at $P < 0.05$ for all analyses.

3. Results

3.1. Sociodemographic and Clinical Characteristics of Ischemic Stroke Survivors

The mean age of the patients was 59.4 ± 15.03 years. Of these patients, 62.9% were men, and 54.7% had a primary school education. Additionally, 73.6% of the participants had a chronic disease. The duration of stroke among patients was 14.16 ± 20.34 months. The mean score on the Acceptance of Illness Scale (AIS) was 20.29 ± 6.35 . Additionally, 88.6% of the participants adhere to their treatment, and the MARS score is 23.33 ± 2.47 . Information regarding other sociodemographic and medical characteristics is provided in Table 1.

3.2. Illness Acceptance Scores According to Sociodemographic and Clinical Characteristics

When comparing participants' illness acceptance scores with their sociodemographic and clinical characteristics,

it was found that illness acceptance scores significantly increased with higher levels of education ($h=6,544$, $P=0,038$) and income ($h=8.464$, $P=0,015$).

Table 1. Sociodemographic and clinical characteristics of stroke patients (n=254)

Characteristics	
Age, years, mean \pm SD	59.40 \pm 15.03
Gender, n (%)	
Female	95 (37.1)
Male	159 (62.9)
Marital status n (%)	
Married	191 (75.2)
Single	63 (24.8)
Education n (%)	
Primary education	139 (54.7)
High School	54 (21.3)
University and above	61 (24.0)
Working status n (%)	
Employed	30 (11.8)
Unemployed/Retire	224 (88.2)
Socioeconomic situation n (%)	
Less income than expenditures	124 (48.8)
Income equals expenditures	95 (37.4)
More income than expenditures	35 (13.8)
Smoker n (%)	
Yes	45 (17.7)
No	128 (50.4)
Quit smoking	81 (31.9)
Comorbidity n (%)	
Yes	187 (73.6)
No	67 (26.4)
Hemiplegic Side	
Right	119 (46.9)
Left	135 (53.1)
Duration of stroke (months) (mean \pm SS)	14.16 \pm 20.34
Medication count, mean \pm SD	4.39 \pm 1.79
AIS, mean \pm SD (8-40)*	20.29 \pm 6.35
MARS, mean \pm SD (5-25)*	23.33 \pm 2.47
MARS n (%)	
Medication adherence	225 (88.6)
Medication non-adherence	29 (11.4)

AIS= acceptance of illness scale, MARS= medication adherence reporting scale, * It shows the lowest and highest scores that can be obtained.

In pairwise comparisons between groups, it was found that illness acceptance was significantly higher among participants with a university or higher education compared to those with primary education ($u=-28.551$, $P=0.011$), and among those with equal ($u=-21.401$, $P=0.032$) or higher income ($u=-35.611$, $P=0.011$) compared to those with lower income. Illness acceptance scores did not vary with other variables (Table 2).

3.3. Correlation between Variables

It was found that there was a significant negative correlation between participants' AIS scores and the Specific Necessity ($\rho=-0.203$, $P=0.001$), Specific

Concern ($\rho=-0.169$, $P=0.007$), and General Overuse ($\rho=-0.193$, $P=0.002$) subscales of the BMQ-T. Additionally, a significant positive correlation was found between AIS and MARS scores ($\rho=0.210$, $P=0.012$). (Table 3).

3.4. Factors Associated With Acceptance of Illness in Participants

In the multiple regression analysis conducted to determine the factors influencing illness acceptance in stroke patients, when considering age, stroke duration, length of hospitalization, total MARS score, Specific Necessity, Specific Concern, General Overuse, and

General Harm variables of the stroke patients participating in the study, it was found that they collectively accounted for 11% of the variance in illness acceptance ($r=0.332$, $r^2=0.110$, $P=0.001$). According to

the regression analysis, the Specific Necessity ($\beta=-0.204$, $P=0.002$) and General Overuse ($\beta=-0.220$, $P=0.001$) subscales of the BMQ-T negatively influenced illness acceptance, respectively (Table 4).

Table 2. Comparison of participants' acceptance of illness scale scores according to sociodemographic and clinical characteristics (n=254)

Characteristics	AIS	Test Statistics	P
	Med (Q1-Q3)		
Gender			
Female	19 (15-23)	-1.667*	0.096
Male	20 (16-26)		
Marital status n (%)			
Married	19 (15-25)	-0.113*	0.910
Single	19 (16-24)		
Education			
Primary school	18 (15-24) ^a	6.544**	0.038 ^{c>a}
High school, college	19 (15.75-24.25) ^b		
University or above	21 (17-27) ^c		
Working status n (%)			
Employed	20 (17.75-25)	-0.943*	0.345
Unemployed/Retire	19 (15-24.75)		
Socioeconomic situation n (%)			
Less income than expenditures	18 (14.25-23) ^a	8.464**	0.015 ^{b>a} ^{c>a}
Income equals expenditures	20 (17-26) ^b		
More income than expenditures	21 (17-26) ^c		
Smoker n (%)			
Yes	18 (15-25)	2.160**	0.340
No	19.50 (15-23)		
Quit smoking	20 (16-26)		
Comorbidity n (%)			
Yes	19 (14.75-25)	-0.730*	0.465
No	20 (16-24)		
Hemiplegic Side			
Right	19 (15-25)	-0.657	0.511
Left	20 (16-25)		
MARS			
Medication adherence	19 (16-25)	-0.432*	0.666
Medication non-adherence	20 (15-24.50)		

*Mann Whitney U Test, ** Kruskal Wallis Test, AIS= acceptance of illness scale, MARS= medication adherence reporting scale.

Table 3. Correlation (Spearman's rho) between variables (n=254)

	1	2	3	4	5	6	7	8
1. Acceptance of Illness Scale	1							
2. Medication Adherence Reporting Scale	0.210*	1						
3. BMQ-Specific Necessity	-0.203**	0.078	1					
4. BMQ- Specific Concerns	-0.169**	-0.103	0.026	1				
5. BMQ-General Overuse	-0.193**	-0.134*	-0.075	0.300**	1			
6. BMQ- General Harm	-0.043	-0.108	-0.237**	0.469**	0.361**	1		
7. Age	-0.083	-0.164**	0.157**	-0.019	0.189**	-0.008	1	
8. Medication count	-0.023	-0.163**	0.137*	0.057	0.101	0.040	0.348**	1
9. Stroke duration	0.044	-0.037	-0.176*	0.024	-0.093	-0.001	-0.206**	-0.053

**Correlation is significant at the 0.01 level, * Correlation is significant at the 0.05 level, BMQ= beliefs about medicine questionnaire.

Table 4. Factors associated with acceptance of illness in participants

	B	β	t	p	CI (%95)
Age	0.005	0.011	0.169	0.866	-0.051-0.061
Duration of stroke	-0.001	-0.002	-0.032	0.975	-0.043-0.042
Number of hospitalizations	0.158	0.047	0.681	0.496	-0.299-0.615
Medication count	0.011	0.003	0.048	0.962	-0.444-0.466
Medication Adherence Reporting Scale	0.019	0.008	0.120	0.905	-0.299-0.338
BMQ-Specific Necessity	-1.284	-0.204	-3.124	0.002	-2.093-(-0.474)
BMQ- Specific Concerns	-0.743	-0.103	-1.425	0.156	-1.770-0.284
BMQ-General Overuse	-1.857	-0.220	-3.234	0.001	-2.988-(-0.726)
BMQ- General Harm	0.253	0.034	0.452	0.652	-0.851-1.358

The symbol B indicates the unstandardized coefficient, and the symbol β indicates the standardized coefficient, CI= confidence interval, BMQ= beliefs about medicine quastionnaire.

4. Discussion

In this study, which aimed to identify the factors influencing illness acceptance in stroke patients, it was found that individuals had a moderate level of illness acceptance, and as acceptance of illness increased, treatment adherence also improved. It was determined that illness acceptance increased with patients' education and income levels increased. An increase in concerns about medications, as well as beliefs that medications were overused and necessary, were associated with a decrease in illness acceptance. It was found that patients' beliefs about medications (Specific Necessity and General Overuse subscales) were significant determinants of illness acceptance.

In studies conducted with elderly individuals with Crohn's disease, colorectal cancer, and chronic illnesses, illness acceptance was reported to be at a moderate level (Kurpas et al., 2013; Kapela et al., 2017; Kowalska et al., 2019; Gawor et al., 2021), while in a study with hypertension patients, it was found to be at a high level (Pluta et al., 2020). In studies with stroke patients, illness acceptance was reported to be low (Kowalska et al., 2016) and moderate (Guzek and Kowalska, 2020). Similarly, in this study, illness acceptance was found to be at a moderate level. Most individuals with stroke face challenges in their social environment, living conditions, adapting to daily life, and coping with sudden disability (Ruksakulpiwat et al., 2020). Studies have shown that illness acceptance is influenced by various factors, such as the type and severity of the stroke, stroke duration, functional status, psychological condition, educational level, and socioeconomic status (Kowalska et al., 2016; Unni and Shiyabola, 2016; Pluta et al., 2020; Guzek and Kowalska, 2020). In this study, it was found that educational level and socioeconomic status had a positive impact on illness acceptance. Educational level may be a factor influencing individuals' ability to understand their illness, evaluate treatment options, and take an active role in the treatment process. Therefore, individuals with higher educational levels are generally more likely to have greater knowledge about health issues and more motivation to manage their illness, which can lead to increased illness acceptance. Similarly, socioeconomic

status can directly affect illness acceptance, as it influences individuals' access to healthcare, the quality of care, and daily living conditions. Thus, the importance of health education should be emphasized, special support programs should be developed for patients from lower socioeconomic backgrounds, and efforts should be made to address inequalities in access to healthcare.

The literature reports that medication adherence rates in individuals with stroke range from 33% to 87% (Sjölander et al., 2013; Kronish et al., 2013; Ruksakulpiwat et al., 2020; Zhang et al., 2021; Arkan et al., 2022). In this study, the adherence rate was found to be high at 88.6%. This may be due to the fact that the patients included in the study had MMSE scores of 24 or higher and that hospitalized patients are required to follow treatment under supervision. High cognitive function may have enabled patients to better understand the treatment plan, grasp its importance, and be more successful in following it. It is also believed that patients who accept their illness will have higher levels of treatment adherence. In this study, it was found that as illness acceptance increased, treatment adherence also improved.

In the study, concerns about medications and the belief that medications are overused were found to be factors that reduce illness acceptance. Contrary to expectations in the literature, a negative relationship was found between the belief that medications are necessary and illness acceptance. Patients' belief in the necessity of medications constitutes the "perceived benefit," while the belief that medications are overused forms the "perceived barrier" (Cinar et al., 2021). When perceived benefits are high and perceived barriers are low, illness acceptance is expected to be high. Conversely, the high illness acceptance among patients who believed medications were necessary in this study may be due to the inclusion of hospitalized individuals. Hospitalized patients perceive medications as necessary because they are required to adhere to medication use under the supervision of nurses and doctors; however, this does not necessarily mean that they have internalized their illness. Furthermore, consistent with the literature (Ruksakulpiwat et al., 2020), beliefs about medication overuse can reduce confidence in treatment, negatively

impact motivation for illness management, and hinder internalization of illness. Therefore, to foster positive medication beliefs, patients should be provided with detailed information about the effects of medications, their purposes of use and role in treatment, potential side effects, and treatment strategies.

5. Conclusion

In this study, patients' beliefs about medications were found to be an important determinant of illness acceptance. Positive beliefs about the effectiveness and necessity of medications can increase treatment adherence and contribute to the prevention of recurrent strokes. Therefore, it is recommended that during hospital admission, discharge, and home visits, illness acceptance, medication beliefs, treatment adherence, and the factors affecting these aspects should be assessed. Personalized intervention models led by nurses should be designed for patients reporting negative beliefs, and the impact of these interventions on illness acceptance, medication beliefs, and treatment adherence should be further investigated, especially in efforts to prevent secondary strokes.

Limitations

This study has several limitations. The use of self-reported questionnaires may have introduced response bias due to the potential misinterpretation of questions, thereby affecting the accuracy of the findings. The primary limitation is that the study was conducted among hospitalized patients, which may have contributed to higher levels of treatment adherence and limited the generalizability of the results. Additionally, while factors such as psychological status, functional status, and stroke severity are important in illness acceptance, these variables were not assessed in the study, which limits the ability to examine all factors that may influence illness acceptance. Despite these limitations, to the best of our knowledge, this study is the first to investigate the impact of medication beliefs and treatment adherence on illness acceptance in individuals with stroke.

Author Contributions

The percentages of the authors' contributions are presented below. All authors reviewed and approved the final version of the manuscript.

	Me.A.	Mu.A.	F.İ.Ç.	E.Y.
C	30	20	30	20
D	50		50	
S	25	25	25	25
DCP	50	50		
DAI	30	20	30	20
L	40	10	40	10
W	30	30	30	10
CR	25	25	25	25
SR	30	20	30	20
PM	40	30	30	30
FA	30	30	30	10

C=Concept, D= design, S= supervision, DCP= data collection and/or processing, DAI= data analysis and/or interpretation, L= literature search, W= writing, CR= critical review, SR= submission and revision, PM= project management, FA= funding acquisition.

Conflict of Interest

The authors declared that there is no conflict of interest.

Ethical Consideration

Ethical approval was obtained from the ethics committee of the hospital where the study was conducted (Ankara City Hospital (approval date: August 17, 2022, protocol code: E2-22-2305).

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