

## Anxiety, Depression Symptoms and their Association with Fatigue in Kidney Transplant Recipients

*Síntomas de Ansiedad y Depresión y su Asociación con la Fatiga en Receptores Adultos de Trasplante de Riñón: Un Estudio Transversal*

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### RESUMEN

**Introducción:** Los síntomas de ansiedad y depresión, así como la fatiga, causan deterioro funcional en los receptores de trasplante renal y, por lo tanto, empeoran su calidad de vida. Sin embargo, esta relación no se ha esclarecido por completo. **Objetivo:** Este estudio se realizó para evaluar los niveles de ansiedad, depresión y fatiga en adultos receptores de trasplante renal y los factores que influyen en estas afecciones. **Material y métodos:** Se utilizó un diseño transversal y descriptivo. El estudio se realizó con 140 adultos receptores de trasplante renal. Los datos se recopilaron mediante un Formulario de Información Personal, la Escala Hospitalaria de Ansiedad y Depresión y la Evaluación Multidimensional de la Fatiga, y se analizaron mediante pruebas descriptivas, paramétricas y no paramétricas. **Resultados:** Se encontró una correlación positiva entre los síntomas de ansiedad y el nivel de fatiga y el estrés que esta causaba. Los síntomas de depresión se correlacionaron positivamente con el índice de fatiga global, así como con todas las subdimensiones de la fatiga. Además, los síntomas de depresión y el índice de masa corporal se identificaron como predictores independientes del

aumento del índice de fatiga global. **Conclusiones:** El estudio destaca la importancia de integrar la relación entre los síntomas de ansiedad y depresión, así como la fatiga, en la atención integral de enfermería para pacientes con trasplante renal.

**Palabras Clave:** ansiedad; depresión; fatiga; trasplante renal; enfermería.

### ABSTRACT

**Background:** Anxiety and depression symptoms, and fatigue cause functional deterioration in kidney transplant recipients and therefore worsen their quality of life. However, this relationship has not been fully clarified. **Objectives:** This study was conducted to evaluate the levels of anxiety and depression symptoms and fatigue in adult kidney transplant recipients and the factors affecting these conditions. **Methods:** A cross-sectional and descriptive design was used. The study was conducted with 140 adult kidney transplant recipients. Data were collected via a Personal Information Form, the Hospital Anxiety and Depression Scale, and the Multidimensional Assessment of Fatigue and analyzed using descriptive, parametric, and nonparametric tests. **Results:** A positive correlation was found

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between anxiety symptoms and both the level of fatigue and the distress it caused. Depression symptoms were positively correlated with the global fatigue index and all fatigue subdimensions. Additionally, depression symptoms and body mass index were identified as independent predictors of increased global fatigue index. **Conclusions:** The study highlights the importance of integrating the relationship between anxiety and depression symptoms, and fatigue into holistic nursing care for kidney transplant recipients.

**Keywords:** anxiety; depression; fatigue; kidney transplant; nursing.

## INTRODUCTION

Kidney transplantation is the most effective treatment option for the majority of patients with end-stage renal disease, and it improves quality of life by enhancing both physical and psychosocial well-being<sup>(1,2,3)</sup>. However, patients face various difficulties in their post-transplant life<sup>(4)</sup>. Following the transplant, recipients face many new problems, such as rejection and fear of infection, complications due to immunosuppressive therapy, and coping with physical changes such as weight gain. All these problems also affect the individual emotionally and can lead to symptoms of hopelessness, fatigue, anxiety, and depression<sup>(5)</sup>. In fact, psychological well-being enables kidney transplant recipients to have a sense of control over their own lives<sup>(6)</sup>. Therefore, psychosocial care provided in accordance with the evaluation results of fatigue, anxiety, and depression in kidney transplant recipients may improve their quality of life by affecting their well-being and adjustment<sup>(7)</sup>.

Although fatigue is common (22-63%) in kidney transplant recipients, it is often underestimated among other problems<sup>(8)</sup>. Both physical and psychological fatigue can have an impact on emotional state. Liu et al.<sup>(9)</sup> also reported that fatigue incidence in kidney transplant recipients is high and is influenced by physical, psychological, and situational factors. Side effects of immunosuppressive drugs also increase the prevalence of psychological factors that contribute to fatigue<sup>(10)</sup>. Increased

fatigue rates and other inhibitory symptoms may result in higher depression and anxiety in kidney transplant recipients. The combination of fatigue, depression, and anxiety contributes to poor clinical outcomes<sup>(4)</sup>. Considering these results, the determination of post-transplant anxiety and depression symptoms and fatigue levels in kidney transplant recipients is important in terms of taking precautions, adjusting to treatment, increasing quality of life, and improving transplant outcomes. Previous studies indicated that anxiety and depression symptoms negatively affected the quality of life<sup>(3,11)</sup> in kidney transplant recipients. A systematic review of kidney transplant recipients also indicated that fatigue was significantly associated with symptoms of depression and/or sleep disorders, was extremely debilitating, and significantly impaired quality of life<sup>(8)</sup>. The identification and effective management of psychological symptoms -particularly anxiety and depression- following kidney transplantation play a critical role in enhancing patients' overall well-being. Although symptoms of fatigue, anxiety, and depression frequently coexist in kidney transplant recipients, the interrelationships among these symptoms and the factors influencing them remain insufficiently understood.

## OBJECTIVES

This study aims to evaluate the levels of anxiety, depression, and fatigue in adult kidney transplant recipients, as well as the relationships among these symptoms and the factors affecting them.

## MATERIALS AND METHODS

### Research Design

This is a descriptive, cross-sectional, and correlational study. In the study, the STROBE checklist, which is used for reporting cross-sectional studies, was followed.

### Setting and Sample

The research was carried out in the organ transplant outpatient follow-up unit of a university hospital that has been in service since 1982. The sample size was calculated using an online application (<http://www.raosoft.com/samplesize.html>) based on the known-population sampling formula. In the organ

transplantation center, a total of 234 kidney transplants were performed in 2019. The sample size was calculated as 132 subjects based on a confidence interval of 95% and a deviation value of 5% by considering the depression findings in transplant patients in the study by Wang et al.<sup>(12)</sup> considering some attrition, it was planned to recruit approximately 10% more of the sample, and therefore the study was carried out with 140 patients. Patients who were aged  $\geq 18$  years and underwent a kidney transplant at least one month ago were included in the study. Multiple organ transplants or multiple kidney transplant procedures were determined as exclusion criteria. Patients who came for follow-up were not asked about their race, religion, or ethnicity. Accepting transplant recipients from all over the country, the center can follow up an average of 100 organ transplant recipients daily on an outpatient basis. Considering these reasons, it can be thought that the population represents the whole country.

### Data Collection

The data were collected by ATC via a single face-to-face interview with adult kidney transplant recipients who met the inclusion criteria and attended the organ transplant outpatient clinic at a university hospital between July 7, 2021, and September 29, 2021, after obtaining ethical approval and institutional permissions. Personal Information Form, Hospital Anxiety and Depression Scale (HADS), and Multidimensional Fatigue Assessment (MAF) were used for data collection.

### Instrument

The Personal Information Form included questions about age, gender, marital status, economic status, employment status, body mass index (BMI), regular exercise, and hospital readmission after transplantation. The Hospital Anxiety and Depression Scale (HADS) is a self-report tool specifically designed to screen symptoms of anxiety and depression in those with physical illness. The Turkish version of the Hospital Anxiety and Depression Scale was used in the study<sup>(13,14)</sup>. It consists of two subscales, each consisting of seven items. Each item is scored 0-3, and the total score is 0-21. Higher scores indicate higher levels of anxiety or depression. In this study, Cronbach's  $\alpha$  was found

to be 0.81 for anxiety and 0.71 for depression. The Multidimensional Assessment of Fatigue (MAF) is a 16-item scale that measures fatigue across five dimensions. The Turkish version of the Multidimensional Assessment of Fatigue Scale was used to evaluate fatigue (MAF-T)<sup>(15)</sup>. The sub-dimensions of the MAF scale are degree, severity, distress, degree of interference in activities of daily living (household chores, cooking, bathing, dressing, working, socializing, sexual activity, leisure and entertainment, shopping, walking, and exercise), and the timing of fatigue (frequency and variability over the past week). The combined score across the five dimensions of fatigue yields the Global Fatigue Index (GFI). Item 16 of the MAF is not included in the GFI. High scores indicate more severe fatigue, fatigue distress, or fatigue-related impairment in activities of daily living. In this study, Cronbach's alpha was 0.93.

### Statistical Analysis

Continuous data were presented as mean $\pm$ standard deviation (SD), and categorical data as frequency (n) and percentage (%). The normality assumptions were tested with the Shapiro-Wilk test. The independent t-test was used to compare total scores between two groups. One-way ANOVA was used to compare total scores across three or more groups, and the Tukey HSD test was used as a post hoc test for significant cases. Pearson and Spearman correlation tests were used to examine the relationship of anxiety, depression, and fatigue with other parameters. Multiple linear regression was performed to identify factors associated with fatigue. The variables with  $p < 0.2$  in the univariate analyses were further tested in the multivariate model. Cronbach's alpha coefficient was calculated for the reliability analysis. Statistical analysis was conducted on the IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY). A two-tailed p-value less than 0.05 was considered statistically significant. Statistical support was received for the research.

### Ethical Considerations

Before starting the study, the approval of the relevant institution's Clinical Research Ethics Committee (25.05.2021-70904504/312), permission from the relevant hospital, and

informed consent from the participants were obtained. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

**RESULTS**

A total of 140 adult kidney transplant recipients with a mean age of 40.51±11.27 years (min-max: 19-75) were included in the study. It was determined that 59.3% of the recipients were male, 67.1% were married, and that 64.3% did not have a job. According to the BMI classification, 36.6% of the patients were in the pre-obesity category, and 19.4% were in the obese category. In addition, 57.9% of patients did not exercise

regularly, and 62.6% had been hospitalized repeatedly.

**Table 1** shows the correlation of anxiety and depression sub-dimensions of the HADS with MAF-GFI and its sub-dimensions. A very weak positive correlation was found between the anxiety sub-dimension of the HADS and the degree of fatigue and distress sub-dimensions of the MAF. The depression sub-dimension of the HADS had a weak positive correlation with the GFI and the degree of fatigue, its severity, and the distress sub-dimensions of the MAF, and a very weak positive correlation with the effect of fatigue on various activities of daily living and the timing sub-dimensions.

**Table 1.** Correlation of Anxiety and Depression with MAF-GFI and its Sub-dimensions (n:140)

	HADS Anxiety		HADS Depression	
	r	p*	r	p*
Multidimensional Assessment of Fatigue Scale Sub-Dimensions				
Global Fatigue Index (GFI)	0.158	0.062	0.322	<0.001
Fatigue Degree	0.193	0.022	0.337	<0.001
Fatigue Severity	0.162	0.056	0.309	<0.001
Fatigue Distress	0.168	0.047	0.319	<0.001
The Degree of Interference in Activities of Daily Living	-0.023	0.785	0.191	0.024
Fatigue Frequency	0.125	0.141	0.196	0.021

HADS: Hospital Anxiety and Depression Scale, \*Pearson correlation test.

In **Table 2**, factors independently associated with GFI were analyzed using multiple linear regression. Variables with p-values <0.2 in univariate analyses were included in the multivariate model. The effect of each independent variable in the model on the dependent variable was evaluated using the standardized regression coefficient (β), holding all other independent variables constant. As a result of the analysis, it was determined that increases in HADS depression score (β=0.361, p<0.001) and BMI (β=0.183, p=0.027) independently increased GFI.

The mean fatigue (GFI) and HADS anxiety scores of patients who were re-hospitalized after transplant were higher

than the scores of those who were not. The mean HADS depression score of the patients who did not have a job was higher and more significant than the scores of those who had a job. The mean HADS depression score of patients who did not exercise regularly was higher than that of those who did, but this difference was not statistically significant (**Table 3**). In addition, although not presented in the table, anxiety symptoms were detected in 11.4% of kidney transplant recipients and depression symptoms in 34.3%. A very weak negative correlation was observed between the anxiety sub-dimension of the HADS and patients' economic status. A very weak positive correlation was determined between fatigue and BMI (**Table 4**).

**Table 2.** Factors Associated with the Global Fatigue Index (n:140)

Model	Global Fatigue Index (GFI)						95% Confidence Interval	
	B	SE	$\beta$	t	Sig.	VIF	Lower	Upper
Age	-0.08	0.087	-0.078	-0.915	0.362	1.162	-0.253	0.093
Male Gender	-3.114	1.943	-0.131	-1.602	0.112	1.069	-6.961	0.733
Working Status	4.247	2.158	0.176	1.968	0.051	1.272	-0.025	8.519
BMI	2.811	1.256	0.183	2.238	0.027	1.070	0.325	5.298
Rehospitalization Status	3.313	1.974	0.137	1.679	0.096	1.064	-0.594	7.220
HADS Anxiety	-0.261	0.281	-0.088	-0.931	0.354	1.431	-0.817	0.294
HADS Depression	1.068	0.277	0.361	3.855	<0.001	1.399	0.520	1.616

R=0.484, R2=0.234, p<0.001

**Table 3.** Comparison of Anxiety, Depression and Fatigue Scores According to Patient Characteristics (n:140)

Variables	n(%)	HADS Anxiety [ $\bar{X} \pm SS$ : 6.36 $\pm$ 3.93 (min-max: 0-20)]			HADS Depression [ $\bar{X} \pm SS$ : 5.57 $\pm$ 3.93 (min-max: 0-16)]			MAF- GFI [ $\bar{X} \pm SS$ : 20.25 $\pm$ 12.01 (min-max: 1-43)]		
		$\bar{X} \pm SS$	Test value	p	$\bar{X} \pm SS$	Test value	p	$\bar{X} \pm SS$	Test value	p
Sex										
Female	57(40.7)	6.44 $\pm$ 3.66	t=0.185	0.854	5.56 $\pm$ 4.06	t=-0.025	0.980	22.01 $\pm$ 12.76	t=1.442	0.151
Male	83(59.3)	6.31 $\pm$ 4.13			5.58 $\pm$ 3.86			19.04 $\pm$ 11.39		
Marital status										
Married	94(67.1)	6.35 $\pm$ 3.75	t=-0.057	0.955	5.43 $\pm$ 3.66	t=-0.586	0.560	19.61 $\pm$ 12.35	t=-0.902	0.368
Single	46(32.9)	6.39 $\pm$ 4.32			5.87 $\pm$ 4.46			21.56 $\pm$ 11.32		
Work Status										
Working	50(35.7)	6.26 $\pm$ 3.98	t=-0.233	0.816	4.66 $\pm$ 3.2	t=-2.237	0.027	22.25 $\pm$ 11.37	t=1.475	0.143
Not working	90(64.3)	6.42 $\pm$ 3.93			6.08 $\pm$ 4.21			19.14 $\pm$ 12.27		
Regular Exercise										
Yes	59(42.1)	5.78 $\pm$ 3.86	t=1.508	0.134	4.86 $\pm$ 4.06	t=1.833	0.069	18.83 $\pm$ 11.77	t=1.190	0.236
No	81(57.9)	6.79 $\pm$ 3.95			6.09 $\pm$ 3.77			21.28 $\pm$ 12.15		
Rehospitalization Status										
Yes	87(62.6)	6.84 $\pm$ 3.88	t=-1.759	0.081	5.95 $\pm$ 3.93	t=-1.416	0.159	22.03 $\pm$ 12.08	t=-2.126	0.035
No	52(37.4)	5.63 $\pm$ 3.96			4.98 $\pm$ 3.91			17.63 $\pm$ 11.3		

t, Independent t-test.

**Table 4.** Correlation of Anxiety, Depression and Fatigue Scores with Various Variables (n:140)

Variables	HADS Anxiety		HADS Depression		MAF-GFI	
	r	p	r	p	r	p
Age	-0.081	0.3391	-0.015	0.8631	-0.096	0.2571
Economic status	-0.175	0.0382	-0.103	0.2272	-0.078	0.3572
Body Mass Index	-0.103	0.2362	-0.001	0.9892	0.182	0.0352
Number of Rehospitalization	0.041	0.7282	0.135	0.2532	0.073	0.5372

1Pearson correlation test, 2Spearman correlation test

## DISCUSSION

This study provides results regarding the levels of anxiety and depression symptoms and fatigue in adult kidney transplant recipients and the factors affecting these variables. Anxiety, depression symptoms, and fatigue are important factors affecting the quality of life of kidney transplant recipients. Barutcu Atas et al.<sup>(16)</sup> reported the presence of anxiety in 23.6% and depression in 44.3% of 106 kidney transplant recipients. In the study by Zhang et al.<sup>(17)</sup>, the prevalence of depressive symptoms among kidney transplant recipients was reported as 21.7%. In this study, the prevalence of anxiety (11.4%) and depression (34.3%) symptoms of the participants was at a considerable level. These differences in measurements may be due to different cultural settings. In addition, the time elapsed since the kidney transplant and medical and economic conditions may also explain these differences. When the results were evaluated in general, the incidence of depressive symptoms was found to be high among kidney transplant recipients, which should not be ignored.

Fewer episodes of depression are associated with treatment compliance in kidney transplant recipients<sup>(18)</sup>. Depressive symptoms also affect adherence to pharmacological treatment<sup>(10,12)</sup>. Periodic screening for depression is important in the kidney transplant process<sup>(19)</sup>. Fatigue and its severity, the distress it creates, and the degree of interference in daily living activities also make it difficult to comply with treatment, which is an integral part of daily life after the transplant. In this study, a positive correlation was found between depression score and fatigue (Table 1). It is important to monitor mood and fatigue to improve kidney transplant recipients' quality of life and maintain their well-being. The three most commonly studied symptoms in kidney transplant recipients were depression, anxiety, and fatigue<sup>(20)</sup>. Fatigue is a subjective feeling of discomfort, defined as experiencing a stressful event, weakness, feeling of exhaustion, and lack of energy, and is accepted as a risk factor for depressive symptoms<sup>(17)</sup>. Elimination of this risk factor is important so that anxiety and symptoms of depression, and fatigue will not turn into a cycle that triggers each other. In addition, it is noteworthy that the increased HADS depression score of the patients in the present study was one

of the factors that independently increased the GFI.

Fatigue is known to be the most bothersome symptom for organ transplant recipients<sup>(21)</sup>. It includes both physical and psychological fatigue<sup>(8)</sup> and can have an impact on the mental state of patients<sup>(8,9)</sup>. It is very common among kidney transplant recipients. In one study, 53.1% of kidney transplant recipients reported fatigue<sup>(9)</sup>. In this study, it was found that the degree of fatigue and the distress it caused were positively related to the HADS anxiety score. It was revealed that there was a positive correlation between the HADS depression score and the GFI, the degree of fatigue, severity, distress, frequency, and the degree of interference in activities of daily living (Table 1). Similar to the results of the present study, Zhang et al.<sup>(17)</sup> reported a significant relationship between fatigue and depression. Considering the negative effects of fatigue and depression on daily functioning and quality of life in kidney transplant recipients, the findings are very significant. It should be kept in mind that anxiety, depression, and fatigue may trigger rejection attacks by negatively affecting the individual's activities of daily living and medication adherence<sup>(22,23)</sup>. The findings of the present study revealed the necessity of evaluating anxiety, depression, and fatigue in kidney transplant recipients before these negative variables turned into a cycle that triggered each other and negatively affected the activities of the individual. However, it's important to note that fatigue can have causes other than symptoms of anxiety and depression. Kidney transplant recipients experiencing fatigue should be evaluated holistically, both physically and psychologically.

Transplant recipients may be frustrated due to many new challenges, including fear of rejection and infection, complex immunosuppressive regimens, and side effects<sup>(5,24)</sup>. Kidney transplant recipients isolating themselves after transplant surgery due to infection anxiety may have decreased social activities and a tendency towards depression<sup>(25)</sup>. Since the increased anxiety after a transplant may cause an increase in catecholamines together with immunosuppressive agents, it may complicate blood sugar regulation and increase the risk of rejection<sup>(26)</sup>. Therefore, determining the

factors associated with anxiety and depression symptoms and fatigue in recipients is important for the prognosis of a disease. In one study, symptom burden-especially fatigue-was associated with depression, profoundly affecting daily activities and psychological state in kidney transplant recipients; and being married was reported to be associated with lower levels of depression symptoms<sup>(2)</sup>. In this study, there was no significant difference between the gender and marital status of kidney transplant recipients and their anxiety, depression symptoms, and fatigue scores, while fatigue was found to be significantly higher in patients with repeated hospitalizations (**Table 4**). It should also be kept in mind that fatigue, anxiety, and depression symptoms may facilitate conditions such as the risk of infection or rejection that cause repeated hospitalization in kidney transplant recipients.

Fatigue has been reported to be associated with symptoms of depression and obesity in transplant recipients<sup>(8)</sup>. Since fatigue and depression are also mentioned as causes of physical inactivity, they also appear as factors that prevent physical exercise, which is important in organ transplant recipients<sup>(27,28)</sup>. Weight gain after a kidney transplant is very common<sup>(29)</sup>. In a study, it was reported that there were negative correlations between BMI and general health, physical activity, and vitality<sup>(30)</sup>. In this study, it was observed that more than half of the patients did not exercise regularly (57.9%) and were above normal weight (56.0%). In addition, it was found that the mean HADS depression score of the patients who did not exercise regularly was higher than that of the patients who did, but it was not statistically significant (Table 3). In the study of Nöhre et al.<sup>(31)</sup>, no significant relationship was found between BMI and mean HADS anxiety and depression scores. However, an increase in BMI and depression can also be seen as factors that cause an increase in atherosclerosis, with the effect of post-transplant immunosuppressive agents. It should also be considered that the increased BMI level in kidney transplant recipients may adversely affect their mental status by increasing inactivity and fatigue. In the present study, it was determined that BMI was one of the factors independently associated with increased fatigue. Employment after a kidney transplant improves individuals' life expectancy

and significantly contributes to mental health and quality of life<sup>(32)</sup>. Returning to work after transplant is an important health indicator, and the rate of depression may increase in recipients who cannot return to their normal lives and work. In this study, the mean HADS depression score of kidney transplant recipients who did not have a job was found to be significantly higher than that of those who did (**Table 3**). In the present study, a negative correlation was also found between the mean HADS anxiety score and economic status. In the study of Jordakieva et al.<sup>(23)</sup>, similar to the results of the present study, it was reported that patients who were unemployed after a kidney transplant experienced more fatigue, anxiety, and depression. Post-transplant return to work has a positive impact on the health and well-being of kidney transplant recipients and on the economic well-being of families and communities<sup>(33)</sup>. In the study, it was determined that the symptoms of anxiety and depression were observed at a substantial rate in kidney transplant recipients and showed positive correlations with fatigue. Considering that depression and BMI increase fatigue independently, it may be recommended that nurses evaluate these three components together and include them in routine screening. Thus, anxiety and depression symptoms, fatigue, and an increase in BMI can be prevented before they become a cycle, and the quality of life of kidney transplant recipients can be improved.

The study provides very important data for kidney transplant recipients. It reveals the necessity of considering anxiety and depression symptoms, fatigue, and BMI together in kidney transplant recipients, which has important effects on increasing individuals' quality of life with a holistic care approach. The research data were based on participants' self-reports, which is a limitation. The data were collected in the outpatient follow-up unit, where patients came for health checkups. In this process, the positive or negative information patients received from their physician about the examination results may have affected their psychological state. This possibility can also be considered a limitation.

## CONCLUSIONS

Kidney transplant is a process that requires special psychological adjustment, although

it increases the quality of life of patients. Some factors, such as maintenance of health, uncertainty about the cost of the disease, and the side effects of drugs, cause significant psychological strain and fatigue after a transplant. However, little is known about the triad of anxiety and depression symptoms and fatigue, which are important determinants of quality of life in kidney transplant recipients, and the factors that influence these variables. In this study, anxiety and depression symptoms were found to be correlated with fatigue. Holistic care, guided by evaluation of outcomes in kidney transplant recipients, can improve quality of life by affecting well-being and adaptation. The results of the study can significantly help healthcare professionals better understand the relationship between anxiety and depression symptoms, fatigue, and BMI in kidney transplant recipients and the planning of the necessary care through holistic assessment.

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#### ETHICS APPROVAL

The research was conducted in accordance with the principles of the Declaration of Helsinki. Before starting the research, approval was obtained from the Akdeniz University Clinical Research Ethics Committee (25.05.2021-70904504/312), and permission was obtained from the institution where the research was conducted.

#### CONSENT TO PARTICIPATE

Before starting the research, Informed consent was obtained from all individual participants included in the study

#### DATA AVAILABILITY STATEMENT

Data supporting the findings of this study can be obtained from the corresponding author upon request from the editor or the referees.

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