# Factors Affecting Admission Frequency and Compliance with Antihypertensive Treatment of Patients Presenting to the Emergency Department with Hypertensive Attack 

# Acil Servise Hipertansif Atak Șikâyeti ile Bașvuran Hastaların Antihipertansif Tedaviye Uyumu ve Bașvuru Sıklğını Etkileyen Faktörler 

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#### Abstract

Aim: Admission to the emergency department (ED) due to a hypertensive attack (HTA) is common. Our study explores patients' compliance with HTA to blood pressure (BP) treatment, the interrelationship of $B P$ values, and their interaction with other factors. Material and Method: Two hundred and sixty seven patients admitted to our ED with the complaint of HTA and previously diagnosed with hypertension were enrolled in this study. During the data collection phase of the study, the Hill-Bone Compliance to High Blood Pressure Therapy Scale (HBCS) and a questionnaire including the sociodemographic characteristics, hypertension-related status, and dietary habits were filled in through face-to-face interviews with the patients. Results: The patients' mean systolic blood pressure (SBP) was 168.77 $\pm 26.83$, and their mean diastolic blood pressure (DBP) was $98.03 \pm 10.44$ at the time of admission. Their mean HBCS score turned out to be 4.78 $\pm 1.79$. The mean HBCS total scores tended to decrease significantly as the level of education increased. The patients restricting their salt intake and going on a diet achieved lower HBCS scores, and the difference between the groups was significant. When the patients' mean SBP and DBP were compared with their HBCS scores, a moderately low correlation was noted between the mean HBCS scores and the mean SBP. Conclusion: The patients with an educational status at the primary school level and below presented lower compliance with treatment. When the HBCS scores were compared in terms of whether the patients went on a diet or not, the mean scores of the dieters turned out to be lower. The patients with high compliance with treatment presented lower SBP and DBP.


Key words: compliance with treatment; hypertensive attack; lifestyle change


#### Abstract

ÖZET Amaç: Acil servise hipertansif atak nedeniyle bașvuran hastalar sık görülmektedir. Çalıșmamız hipertansif atak ile bașvuran hastaların tansiyon tedavisine uyumunu ve tansiyon değerlerinin birbirleriyle ve diğer faktörlerle olan ilișkisini incelemeyi amaçlamaktadır.

Materyal ve Metot: Bu çalıșmaya acil servisimize hipertansif atak șikâyeti ile bașvuran ve daha önce hipertansiyon tanısı almıș 267 hasta dâhil edildi. Araștırmanın veri toplama așamasında, Hill-Bone Hipertansiyon Tedavisine Uyum Ölçeği (HBHTUÖ -HBCS) ile hastaların sosyodemografik özelliklerini, hipertansiyonla ilgili durumlarını ve beslenme alıșkanlıklarını içeren bir anket hastalarla yüz yüze görüșülerek dolduruldu. Bulgular: Hastaların acil servise bașvurduklarında sistolik tansiyon ortalaması 168,77 $\pm 26,83$; diyastolik tansiyon ortalaması $98,03 \pm 10,44$ 'dur. Katılımcıların ortalama HBHTUÖ puan ortalaması 4,78 $\pm 1,79$ 'dur. Hill-Bone hipertansiyon tedavisine uyum ölçeği total puan ortalamaları eğitim seviyesi arttıkça anlamlı olarak daha düșük bulunmuștur. Diyet haricinde tuz kısıtlaması yapan hastalarda HBHTUÖ puanları ortalaması daha düșük bulunmuștur ve gruplar arasındaki fark anlamlıdır. Hill-Bone hipertansiyon tedavisine uyum ölçeği ile hastaların ortalama sistolik ve diyastolik tansiyonları korelasyon açısından karșılaștııılığında HBHTUÖ puanları ortalaması ile sistolik tansiyon ortalaması arasında orta düșük düzeyde korelasyon saptanmıștır. Sonuç: Eğitim durumları ilköğretim ve altı düzeyinde hastaların tedaviye uyumu daha düșük bulunmuștur. Hastaların diyet yapıp/ yapmama açısından HBHTUÖ puanları karșılaștırıldığında diyet yapan hastaların puan ortalamasının daha düșük olduğu görülmüștür. Tedaviye uyumu yüksek olan hastaların sistolik ve diyastolik tansiyonu daha düșük bulunmuștur.


Anahtar Kelimeler: hipertansif atak; tedavi uyumu; yașam tarzı değișikliği

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## Introduction

$35 \%$ of the world population is afflicted with hypertension (HT), which is considered a major risk factor for cardiovascular diseases and causes the highest rate of death ${ }^{1}$. Hypertension is defined as $140 / 90 \mathrm{mmHg}$ and above by the European Society of Cardiology guidelines and $130 / 80 \mathrm{mmHg}$ and above by the guidelines of the American Heart Association ${ }^{2,3}$.

Roughly 15 to 16 million inhabitants in Türkiye are estimated to suffer from HT. According to an updated systematic review in 2015, 22.1\% of adults aged 18 years and older worldwide were diagnosed with HT. When it comes to Türkiye, its prevalence has been established as $20.3 \%$ in both genders ${ }^{4}$.
Though the exact etiology of primary HT has not been fully elucidated, it is considered to be associated with risk factors, such as age, obesity, race, family history, high sodium diet, decreased nephron count, less physical exercise, and excessive alcohol consumption ${ }^{5-13}$.

Hypertensive attack (HTA) is defined as hypertension with no risk of end-organ damage in individuals without severe blood pressure (BP) elevations who are aged under 60 years with BP above 140/90 and in those aged 60 years and older with BP above $150 / 90^{14}$.

In order to achieve success in the treatment of HT, sufferers are supposed to strictly comply with medical treatment, implement lifestyle changes properly, have periodic examinations on time, and monitor their BP as prescribed ${ }^{15,16}$. However, a number of factors impair compliance with treatment in hypertensive patients. Lifestyle changes coupled with administration of medical treatment methods are of great importance in the treatment of HT.

Thus far, many different scales have been developed to evaluate compliance with treatment in patients. Among these scales is the Hill-Bone Compliance to High Blood Pressure Therapy Scale (HBCS), developed by Kim et al. in $20000^{17}$. This scale includes three important behavioral domains of HT treatment, such as reduced sodium intake, appointment keeping, and medication taking. It can be considered a preferable scale to evaluate the management of individuals with essential HT with respect to drug therapy and lifestyle changes. The validity and reliability of the scale in Turkish was assessed by Karademir et al. ${ }^{18}$.

In the present study, we administered the HBCS, which enabled us to evaluate medical compliance,
nutritional compliance, and total compliance separately. HBCS, which explores the potentiality of patients to comply with treatment through questions about the causes of non-compliance, was administered to the patients presenting to our emergency department (ED) with complaints of HTA. The importance of this study lies in the fact that it is a first step towards measuring hypertensive patients' compliance with HT treatment and their awareness level about HT.

## Materials and Methods

## Study Design

The HBCS and a questionnaire form including sociodemographic characteristics as well as the diagnosis, follow-up, and treatment of the participants' HT disease were administered to collect the data in our study. In addition, the BP of the patients was measured over the brachial artery with a digital device (Nihon Kohden ${ }^{\circ}$ BSM-2301K) calibrated in accordance with the rules, and the measurements were recorded in the form. The questionnaire consisting of 37 questions in total was administered to the respondents through face-to-face interviews.

This descriptive study was conducted on the patients admitted to the ED of a tertiary hospital in Denizli, Türkiye due to HTA complaints between July and August 2022. The prior calculation of the sample size revealed that at least 215 subjects were required for the current study, assuming that the confidence interval was $90 \%$, and that the prevalence was $27.3 \%$. All the HTA patients who matched the research criteria and agreed to participate in the study between the specified dates were recruited for the study. Those over 18 who were diagnosed with HT and presented with HTA complaints were enrolled in the study, whereas those under 18 who suffered from cognitive impairment and the patients who did not agree to participate were excluded. Verbal consent was obtained from the recruited patients. Moreover, the study was initiated after granting the approval from the local ethics committee (approval number and date: 60116787-020/1958/2022). The sociodemographic data and scale scores of the enrolled patients were noted down in the questionnaire form through face-to-face interviews.

## Data Collection

In order to collect the study data, we administered the HBCS along with a questionnaire including the
sociodemographic characteristics created as a result of the literature review and the questions about the diagnosis, follow-up, and treatment of the subjects' HT disease. The HBCS includes 14 items designed in a 4 -point response pattern: (0) "None of the time", (1) "Some of the time", (2) "Most of the time", and (3) "All of the time". All of the items are constructed in the form of negative questions, except for the 6th question which was reverse coded. In the evaluation phase, the sum of all the questions is taken for the total score; that of $1,2,9,10,11$, 12,13 and 14 th items is taken for the subscale of medication taking; that of 3, 4 and 5th items is taken for the subscale of reducing sodium intake; that of the 6,7 and 8th items is taken for the subscale of appointment keeping. In addition, the patients' BP was measured over the brachial artery with a digital sphygmomanometer calibrated in accordance with the rules in the Hypertension Diagnosis and Treatment Guideline, and noted down in the questionnaire form. The questionnaire form consists of 37 questions in total (including the 14 -item scale). The enrolled patients were interviewed face-to-face by the family medicine research assistant and the emergency medicine research assistants.

## Data Analysis

All the collected data were subjected to statistical analysis with IBM Statistical Package for Social Sciences (SPSS) program version 22 package program. The conformity of the variables to the normal distribution was investigated using visual (histogram and probability graphs) and analytical methods (KolmogorovSmirnov / Shapiro-Wilk tests). The descriptive analyses were presented as mean and standard deviations for parametric variables, as median and interquartile differences for non-parametric variables, and as frequency tables for ordinal variables. A Chi-square test was used to compare categorical variables, while t-test and ANOVA analysis of variance were performed for normally distributed variables. Mann-Whitney $U$ and Kruskal-Wallis tests were performed in the analysis of non-parametric variables. A Pearson Correlation test was used to calculate the correlation of numerical variables. The significance level was set at $\mathrm{p}<0.05$ for all the statistical analyses.

## Results

The demographic information of the study population reveals that $47.9 \%(n=128)$ of the subjects were women, and $52.1 \%(n=139)$ were men. The mean age of all

Table 1. Overall characteristics of the subjects

|  | $\mathrm{n}(\%)$ |
| :--- | :---: |
|  | $267(100)$ |
| Gender |  |
| Female | $128(47.9)$ |
| Male | $139(52.1)$ |
| The longest residence |  |
| Province | $123(46.1)$ |
| Town | $83(31.1)$ |
| Village | $61(22.8)$ |
| Marital status |  |
| Single | $10(3.7)$ |
| Married | $209(78.3)$ |
| Divorced/Non-cohabiting | $48(18)$ |
| Educational status |  |
| Illiterate | $14(5.2)$ |
| Literate | $31(11.6)$ |
| Primary school | $108(40.4)$ |
| Secondary school | $39(14.6)$ |
| High school | $46(17.2)$ |
| College/University | $29(10.9)$ |
| Social security |  |
| Social Insurance Institution (SII) | $83(31.1)$ |
| Insuranced Self-Employed Institution (ISEI) | $88(33)$ |
| Government Retirement Fund (GRF) | $75(28.1)$ |
| Private insurance | $4(1.5)$ |
| Green card | $12(4.5)$ |
| Not entitled to social security | $5(1.9)$ |
| Age (Mean $\pm$ S. D.) | $62.60 \pm 10.26(41-88)$ |
| Systolic blood pressure | $168.77 \pm 26.83$ |
| (Mean $\pm$ S. D.) |  |
| Diastolic blood pressure | $98.36 \pm 10.59$ |
| (Mean $\pm$ S. D.) |  |
| Hill-Bone Compliance to High Blood Pressure | $4.78 \pm 1.79$ |
| Therapy Scale (HBCS) (Mean $\pm$ S. D.) |  |
|  |  |

the subjects turned out to be $62.60 \pm 10.21$. Besides, $46.1 \%(\mathrm{n}=123)$ resided in the city center, $78.3 \%$ ( $\mathrm{n}=209$ ) were married, $40.4 \%$ were primary school graduates, and $33 \%$ were entitled to social security.

Their mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) at the time of admission were measured as $168.77 \pm 26.83$ and $98.03 \pm 10.44$, respectively. Their mean HBCS score was calculated as $4.78 \pm 1.79$ (Table 1). Moreover, $59.2 \%$ were nonsmokers, and $52.3 \%$ had never consumed alcohol before. In relation to chronic conditions, $47.9 \%$ had an underlying comorbid disease, and diabetes mellitus ( $\mathrm{n}=56$ ) was the most prevalent comorbid disease (Table 2).

Table 2. Breakdown of subjects' habits and comorbidities

|  | n (\%) |
| :---: | :---: |
|  | 267(100) |
| Smoking |  |
| Yes <br> Smoked but quit <br> № | $\begin{gathered} 36(13.5) \\ 73(27.3) \\ 158(59.2) \end{gathered}$ |
| Alcohol consumption |  |
| Yes <br> Drank but quit № | $\begin{gathered} 46(17) \\ 55(20.7) \\ 166(62.3) \end{gathered}$ |
| Comorbidity |  |
| Yes | 128 (47.9) |
| Comorbid disease |  |
| Diabetes mellitus <br> Coronary artery disease <br> Hyperlipidemia <br> Asthma <br> Chronic renal failure | $\begin{gathered} 56(21) \\ 53(19.9) \\ 17(6.4) \\ 10(3.7) \\ 9(3.4) \end{gathered}$ |
| Lifestyle changes in Hypertension (HT) |  |
| Dieting <br> Yes <br> No | $\begin{aligned} & 181 \text { (67.8) } \\ & 86(32.2) \end{aligned}$ |
| Reduced sodium intake |  |
| Yes | 225 (84.3) |
| No | 42 (15.7) |
| Regular exercise |  |
| Yes | 161 (60.3) |
| No | 106 (39.7) |
| Duration of HT disease |  |
| $\begin{aligned} & 1 \text { year } \\ & 1-10 \text { years } \\ & 10^{+} \text {years } \\ & \hline \end{aligned}$ | $\begin{gathered} 16(6) \\ 159(59.6) \\ 92(39.5) \end{gathered}$ |
| Regular blood pressure (BP) measurement |  |
| 1-3 times a month 1-6 times a week Every day Never | $\begin{gathered} 74(28.6) \\ 104(38.1) \\ 70(26.2) \\ 19(7.1) \end{gathered}$ |
| Medications taken |  |
| Angiotensin converting enzyme (ACE) inhibitor <br> Angiotensin receptor blocker <br> Ca-channel blocker <br> Beta blocker <br> Diuretic | $\begin{gathered} 152(56.9) \\ 89(33.3) \\ 62(23.2) \\ 45(16.9) \\ 40(15) \end{gathered}$ |

The findings suggest that $34.5 \%(\mathrm{n}=92)$ had been suffering from HT for more than 10 years. In addition, $67.8 \%$ began to go on a diet after being diagnosed with HT, while $84.3 \%$ started to reduce their salt intake. The obtained findings also reveal that $60.3 \%$ reported to walk for at least 30 min a day once or twice a week, and that $39.5 \%$ had been afflicted with HT for more than 10 years. It should be also noted that $38.1 \%$ reported to measure their BP at home at least once a week. The
most widely-used BP medication by patients was ACE inhibitors ( $56.9 \%$ ), and $35.2 \%$ were taking more than one antihypertensive medicines (Table 2).

The socio-demographic information of the patients did not yield a significant difference with respect to gender, diet, and reduced sodium intake ( $p>0.05$ ). However, the comparative analysis of these factors in terms of educational status and social security revealed a significant difference ( $\mathrm{p}<0.05$ ). As far as marital status is concerned, only reduced sodium intake was significant, with singles paying the least attention to salt restriction ( $\mathrm{p}<0.05$ ). Another point to highlight was that, as the education level increased, more attention was paid to diet and reduced sodium intake. It was observed that patients with Social Insurance Institution (SII) and Government Retirement Fund (GRF) as social security follow these recommendations more. When patients were categorized as those under 60 years of age and over 60 years of age, there was no significant difference in $\operatorname{diet}$ ( $p>0.05$ ). Furthermore, a significant difference was observable in terms of reduced sodium intake, and those under 60 years of age seemed to attach more importance to this point ( $\mathrm{p}<0.05$ ).

When the HBCS scores were compared based on sociodemographic characteristics, no significant difference was evident, despite the gender-wise superiority in favor of women. Considering the total mean scores of HBCS by place of residence where the subjects had lived for the longest time, village had the highest score. As the population of the place of residence increased, the HBCS score decreased significantly. The HBCS scores did not differ significantly, based on the marital status of the subjects. However, the mean total HBCS scores differed significantly in terms of educational status. The mean total HBCS scores proved to be significantly lower as the level of education increased. When the HBCS scores were compared based on the duration of HT disease, the patients afflicted with HT for more than 10 years had higher scores than the other two groups, and a statistically significant difference was observed (Table 3). In addition, the subjects were asked to report whether they had made any lifestyle changes in terms of HT after being diagnosed with HT. When the HBCS scores of the dieters and non-dieters were compared, the mean score of the dieters turned out to be lower, which also yielded a significant difference. Moreover, the subjects who restricted their salt intake in addition to dieting were observed to have more reduced HBCS scores, and the difference between the groups was statistically significant.

Table 3. Evaluation of HBCS total score averages based on sociodemographic data

|  | n | HBCS Total Score <br> (Mean $\pm$ SD) | p |
| :---: | :---: | :---: | :---: |
| Gender |  |  |  |
| Female | 128 | $4.96 \pm 1.97$ | 0.110* |
| Male | 139 | $4.61 \pm 1.59$ |  |
| The longest residence |  |  |  |
| Province | 123 | $4.29 \pm 1.89$ | $<0.001 * *$ |
| Town | 83 | $4.87 \pm 1.60$ |  |
| Village | 61 | $5.63 \pm 1.45$ |  |
| Marital status |  |  |  |
| Single | 10 | $4.60 \pm 2.41$ | $0.191^{* * *}$ |
| Married | 209 | $4.69 \pm 1.63$ |  |
| Divorced/Non-cohabiting | 48 | $5.16 \pm 1.84$ |  |
| Educational status |  |  |  |
| Illiterate | 14 | $7.93 \pm 1.21$ | $<0.001^{* * *}$ |
| Literate | 31 | $6.26 \pm 1.26$ |  |
| Primary school | 108 | $5.44 \pm 1.19$ |  |
| Secondary school | 39 | $4.18 \pm 1.00$ |  |
| High school | 46 | $3.17 \pm 1.04$ |  |
| College/University | 29 | $2.59 \pm 1.05$ |  |
| Duration of HT disease |  |  |  |
| 1 year | 16 | $5.12 \pm 1.78$ | 0.002** |
| 1-10 years | 159 | $4.48 \pm 1.74$ |  |
| $10^{+}$years | 92 | $5.22 \pm 1.77$ |  |
| Comorbidity |  |  |  |
| Yes | 128 | $5.12 \pm 1.75$ | 0.003* |
| No | 139 | $4.47 \pm 1.77$ |  |

The subjects who had walked for 30 minutes or longer a day had lower HBCS scores than their counterparts who did not take any exercise, resulting in a significant difference (Table 4).

When the mean SBP and DBP values of the patients were compared with their HBCS scores, a moderately low correlation was noted between the mean HBCS scores and the mean SBP. In a similar vein, a low correlation was noted between the mean HBCS scores and the mean DBP. Furthermore, SBP were strongly correlated with DBP, which also indicated significant difference (Table 5).

## Discussion

This study made use of HBCS, which provides researchers with the opportunity to assess compliance with HT treatment. In contradiction with earlier findings, the enrolled women in our study outnumbered

Table 4. Evaluation of the subjects' habits and their HBCS total score averages

| Lifestyle changes in HT | n | HBCS Total Score <br> Mean $\pm$ SD | p |
| :--- | :--- | :--- | :--- |
| Dieting |  |  |  |
| Yes | 181 | $4.43 \pm 1.82$ | $<0.001^{*}$ |
| No | 86 | $5.51 \pm 1.47$ |  |
| Reduced sodium intake |  |  | $<0.001^{*}$ |
| Yes | 225 | $4.48 \pm 1.74$ |  |
| No | 42 | $6.40 \pm 0.99$ | $<0.001^{*}$ |
| Regular exercise |  |  |  |
| Yes | 161 | $4.43 \pm 1.72$ |  |
| No | 106 | $5.30 \pm 1.76$ |  |
| * Obtained from Independent Samples 5 -Test; ** Obtained from Kruskal-Wallis test; HBCS: Hill- |  |  |  |
| Bone Compliance to High Blood Pressure Therapy Scale; HT: Hypertension |  |  |  |

Table 5. Evaluation of the subjects' HBCS total scores

|  | Mean | S. D. | 1 | 2 | 3 |
| :--- | :---: | :---: | :---: | :---: | :---: |
| 1- HBCS $^{(1)}$ | 4.78 | 1.79 | ๆ | $0.305^{\star}$ | 0.239 |
| 2- SBP $^{(2)}$ | 168.77 | 26.83 | $0.305^{\star}$ | ๆ | $0.775^{\star}$ |
| 3- DBP $^{(3)}$ | 98.03 | 10.44 | $0.775^{\star}$ | $0.239^{\star}$ | ๆ |

${ }^{(1)}$ HSBC: Hill-Bone compliance to high blood pressure therapy scale; ${ }^{(2)}$ SBP: systolic blood pressure; ${ }^{(3)}$ DBP: diastolic blood pressure; * $\mathrm{p}<0.001$
the male subjects ${ }^{18}$. Our findings revealed that gender did not play a significant role in HBCS scores, which broadly supports the work of other studies addressing this issue. Furthermore, no significant relationship was observed between marital status and compliance with treatment. What is also revealed by our results is that, as the place of residence increased in population, compliance with treatment proved higher. This may have occurred because residing in a place with larger population facilitates both access to health institutions and follow-up of the disease.
Education-wise, the largest majority of our subjects were comprised of primary school graduates. Our further analyses indicated that compliance with treatment proved to be lower among those whose educational status was at primary school level and below. This leads us to conclude that, as the education level of the patients increases, so does compliance with treatment. Our findings are in accord with those of other recent studies revealing that illiterate patients tend to have lower compliance with treatment ${ }^{15}$.

As identified by other clinical research, HT patients paying special attention to their diet and being careful to add less salt to their meals after being diagnosed with

HT are likely to have more increased compliance with HT treatment ${ }^{19-21}$. Our study likewise showed that the patients restricting their salt intake and going on a diet after the HT diagnosis manifested higher compliance with treatment.

Another point deserving attention in our study is that the patients with higher compliance with drug tended to have more reduced SBP and DBP. In accordance with the present results, several lines of evidence have demonstrated that patients with higher compliance have more reduced SBP and DBP ${ }^{22,23}$. We also observed lower compliance with treatment in the cases where the duration of HT diagnosis exceeded 10 years. Another study similar to ours reports conflicting results, suggesting that a higher compliance with treatment occurs when the treatment period is prolonged ${ }^{24}$.
We found that those with underlying comorbid diseases had more reduced compliance with treatment. Contrary to our study, many clinical studies have shown that comorbidities accompanying HT increase compliance with treatment ${ }^{24-27}$. This finding in our study may be because patients who have to take too many drugs become tired of using this amount of medication continuously, thus not paying adequate attention to treatment.

Hypertension is a growing public health problem of both local and international concern due to its complications, increasing morbidity, and mortality. The presence of patients whose BP is not taken under control is multiplying in Türkiye, which also leads an increasing number of sufferers to present to the ED with HTA. In order to ensure BP compliance in HT, it is critical to comply with the recommended treatment and be mindful of lifestyle changes. Parameters, such as duration of HT diagnosis, salt restriction, and diet can be cited as some of the factors that could impact on compliance with treatment. In our study, compliance with treatment proved to be low, complicating BP control in general and causing the BP values to be high.

We propose that more comprehensive studies should be undertaken on compliance with treatment in HT. This pioneering research has given rise to many questions in need of further investigation. Informing patients about lifestyle changes, questioning the factors that affect their compliance with treatment, and making the required changes in this regard may yield more fruitful results in combating HTA.

## Ethics Committee Approval

The study was initiated after granting the approval from the local ethics committee (approval number and date: 60116787-020/1958/2022).

## Authorship Contributions

Concept: A. Y., U. C., C. U. Design: A. Y., U. C., C. U., Y. K. C. Data Collection or Processing: A. Y., U. C., C. U., Y. K. C., A. O., M. S., M. O, I. T., G. O. Y., M. U., A. K. Analysis or Interpretation: Y. K. C., A. K. Literature Search: A. Y., U. C., C. U., Y. K. C., A. O., M. S., M. O, I. T., G. O. Y., M. U., A. K. Writing: A. Y., U. C., C. U., Y. K. C.

## Financial Disclosure

The author received no specific funding for this work.

## Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

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