ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.5336/cardiosci.2021-81580

Adherence to Anti-hypertensive Treatment in Geriatric Patients: A Systematic Review and Meta-analysis

Geriatrik Hastaların Anti-hipertansif Tedaviye Uyumu: Sistematik Derleme ve Metaanaliz

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ABSTRACT Objective: This study was planned for the systematic review and meta-analysis of the studies evaluating adherence to anti-hypertensive treatment in geriatric patients. **Material and Methods:** Google Scholar, Web of Science, PubMed, CINAHL, MEDLINE and Scopus databases were searched using the keywords "Geriatric, Geriatric patients, Elderly, Elderly patients, Hypertension, Anti-hypertensive agents, Drug compliance". A total of 13 studies were included in the meta-analysis. The included studies were evaluated with the quality evaluation criteria proposed by Polit and Beck. The agreement between the researchers was measured by the kappa test for agreement. The odds ratio was used for effect sizes, Cochran's Q test was used for heterogeneity, the funnel plot and Kendall's tau coefficient were used for publication bias. **Results:** Age, gender, educational status, income level, place of residence and presence of comorbid diseases that affect adherence to anti-hypertensive treatment in geriatric patients were examined. The fact that age and presence of comorbid diseases decreased adherence to anti-hypertensive treatment (OR <1) while being a resident of the city, high educational status, and income level increased adherence to anti-hypertensive treatment (OR >1) in geriatric patients was confirmed by the meta-analysis. **Conclusion:** The factors affecting adherence to anti-hypertensive treatment in geriatric patients were found to be similar to the literature. In contrast to the literature, it was found that gender did not affect adherence to anti-hypertensive treatment in any way. This difference was thought to be due to the lack of homogeneity in the samples of the studies.

Keywords: Aged; hypertension; anti-hypertensive agents; treatment adherence

ÖZET Amaç: Bu çalışma, geriatrik hastalarda anti-hipertansif tedaviye uyumu değerlendiren araştırmaların sistematik derlemesi ve meta-analizi amacıyla planlandı. **Gereç ve Yöntemler:** Google Scholar, Web of Science, PubMed, CINAHL, MEDLINE ve Scopus veri tabanlarında "Geriatria, Geriatric patients, Elderly, Elderly patients, Hypertension, Anti-hypertensive agents, Drug compliance" ile tarama yapıldı. Toplam 13 araştırma, meta-analiz kapsamına alındı. Dâhil edilen araştırmalar, Polit ve Beck tarafından önerilen kalite değerlendirme ölçütleri ile değerlendirildi. Araştırmacılar arası uyum, kappa uyum analizi ile ölçüldü. Etki büyüklükleri için olasılık oranı [odds ratio (OR)], heterojenlik için Cochran Q testi, yayın yanlılığı için huni saçılım grafiği ve Kendall tau katsayısı kullanıldı. **Bulgular:** Geriatrik hastalarda, anti-hipertansif tedaviye uyumu etkileyen yaş, cinsiyet, eğitim durumu, gelir düzeyi, yaşanılan yer ve komorbid hastalığa sahip olma durumları incelendi. Geriatrik hastalarda, yaş ve komorbid hastalığa sahip olma durumunun, anti-hipertansif tedaviye uyumu azaltırken (OR <1); yaşanılan yerin şehir olması, eğitim ve gelir düzeyinin yüksek olmasının anti-hipertansif tedaviye uyumu artırdığı (OR >1) meta-analiz sonucu doğrulandı. **Sonuç:** Geriatrik hastalarda, anti-hipertansif tedaviye uyumu etkileyen faktörlerin, literatür ile benzer olduğu tespit edildi. Literatürün aksine cinsiyetin, anti-hipertansif tedaviye uyumu herhangi bir şekilde etkilemediği tespit edildi. Bu farkın, çalışmaların örneklemlerinde homojenliğin olmamasından kaynaklanacağı düşünüldü.

Anahtar Kelimeler: Yaşlı; hipertansiyon; anti-hipertansif ilaçlar; tedavi uyumu

Blood pressure is the pressure that the blood pumped from the heart to the whole body makes on the vessel wall. Like height and weight, blood pressure is a continuous biological variable. The exact cut-off threshold separating normotension from hypertension is not clear. The relationship between blood pressure level and cardiovascular risk makes the quantification and classification of hypertension

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Peer review under responsibility of Turkiye Klinikleri Cardiovascular Sciences.

Received: 27 Jan 2021 ***Received in revised form:*** 25 Mar 2021 ***Accepted:*** 29 Mar 2021 ***Available online:*** 07 Apr 2021

difficult. Therefore, hypertension is generally defined as the level of arterial blood pressure that doubles the long-term cardiovascular risk.[1]

According to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7), 120-80 mm/Hg is the normal blood pressure for adults over 18 years of age, whereas prehypertension is defined as when the diastolic blood pressure is between 80-89 mm/Hg or systolic blood pressure is between 120-139 mm/Hg.[2]

The diagnosis of hypertension should be rechecked again, usually 1-4 weeks after the first measurement. In general, hypertension is diagnosed by two measurements on different days. If systolic blood pressure is ≥140 mmHg on both days and/or diastolic blood pressure is ≥90 mmHg on both days, hypertension is diagnosed.[3]

Physiopathological changes occur in the vascular structure of geriatric patients. Structural changes are observed in the aorta and large arteries. The vessel wall thickens, and vascular pressure increases. This results in an increase in systolic blood pressure and pulse pressure (isolated systolic hypertension). Meanwhile, vascular resistance also increases and makes diastolic blood pressure elevated (hypertension with disproportionately high systolic blood pressure). Calcification occurs in the vessels, elastin fibers are destroyed, collagen decreases, and arteriosclerosis begins. The elasticity of the vessels and glomerular filtration rate decrease. Therefore, deterioration occurs in sodium excretion. As a result, salt sensitivity increases. The renin-angiotensin mechanism is broken down due to impaired renal function, and excessive renin secretion stimulates aldosterone production, causing increased blood pressure.[4] Due to these reasons, hypertension is a very important risk factor for cardiovascular morbidity and mortality in geriatric patients. It is an important and often asymptomatic chronic disease that requires an anti-hypertensive treatment to reduce the risks of renal problems, cardiovascular and cerebrovascular diseases and permanent adherence to treatment.[5]

Physiopathological changes in geriatric patients increase the risk of hypertension. Therefore, anti-hypertensive treatment is the only option to minimize these risks in geriatric patients. Also, patient adherence to treatment is very important for the effectiveness of the treatment.[4] Geriatric patients have to receive many medications at the same time due to their chronic diseases. The majority of geriatric patients have problems with treatment adherence.[6] It is often seen when the follow-up is not performed well, they do not understand the treatment procedure, do not believe in the strength of the treatment, forget to take adequate doses of medications, or do not consciously take their medications. Factors such as having multiple diseases and reduction of cognitive and functional capacities decrease treatment adherence in geriatric patients.[7] This study was planned for the systematic review and meta-analysis of the studies evaluating adherence to anti-hypertensive treatment in geriatric patients.

The research questions determined in the meta-analysis of the studies evaluating adherence to anti-hypertensive treatment in geriatric patients were as follows:

1) What are the factors affecting adherence to anti-hypertensive treatment in geriatric patients with hypertension?

2) Do age and gender affect adherence to anti-hypertensive treatment in geriatric patients?

3) Do educational status, income level, and place of residence affect adherence to anti-hypertensive treatment?

4) How does having comorbid diseases affect adherence to anti-hypertensive treatment in geriatric patients?

MATERIAL AND METHODS

SELECTION OF THE STUDIES

Firstly, keywords found in the Medical Subject Headings 2019 thesaurus were determined for the literature search. Google Scholar, Web of Science, PubMed, CINAHL, MEDLINE and Scopus databases were searched using the keywords “Geriatric, Geriatric patients, Elderly, Elderly patients, Hypertension, Anti-hypertensive agents, Drug compliance”. The studies included in the meta-analysis were se-

lected according to the criteria of being conducted between the years of 2015-2019, full-text accessibility, being published in academic journals, having an age criterion of over 65 years, and being randomized controlled trials as study design according to the searched database. Reviews, master's and doctoral theses, oral presentations, posters, and qualitative studies were excluded from the meta-analysis.

The systematic review was carried out according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses Statement).[8] The meta-analysis was carried out according to MOOSE (Meta-analysis of Observational Studies in Epidemiology) criteria.[9] The selection process of the studies is shown in the PRISMA scheme (Figure 1). Three hundred sixty studies selected according to the inclusion criteria were evaluated in terms of title, abstract, and content by two researchers (EÖA, FÇ). As a result, 13 studies were included in the meta-analysis. Twelve of the research quality evaluation criteria proposed by Polit and Beck were used in the quality evaluation of these studies.[10] The studies were evaluated and scored by the researchers according to each evaluation criterion. An article with a total score of 0-4 was evaluated as a low-quality article, an article with a total score of 5-9 was evaluated as a moderate-quality article, and an article with a total score of 9-12 was evaluated as a high-quality article. Afterward, they were analyzed for agreement between the researchers.

STATISTICAL ANALYSIS

The meta-analysis was carried out by using the comprehensive meta-analysis software program and SPSS 26 package program. The agreement between researchers was measured by the kappa test for agreement. A kappa agreement rate between 0.20-0.40 shows a low agreement, a kappa agreement rate be-

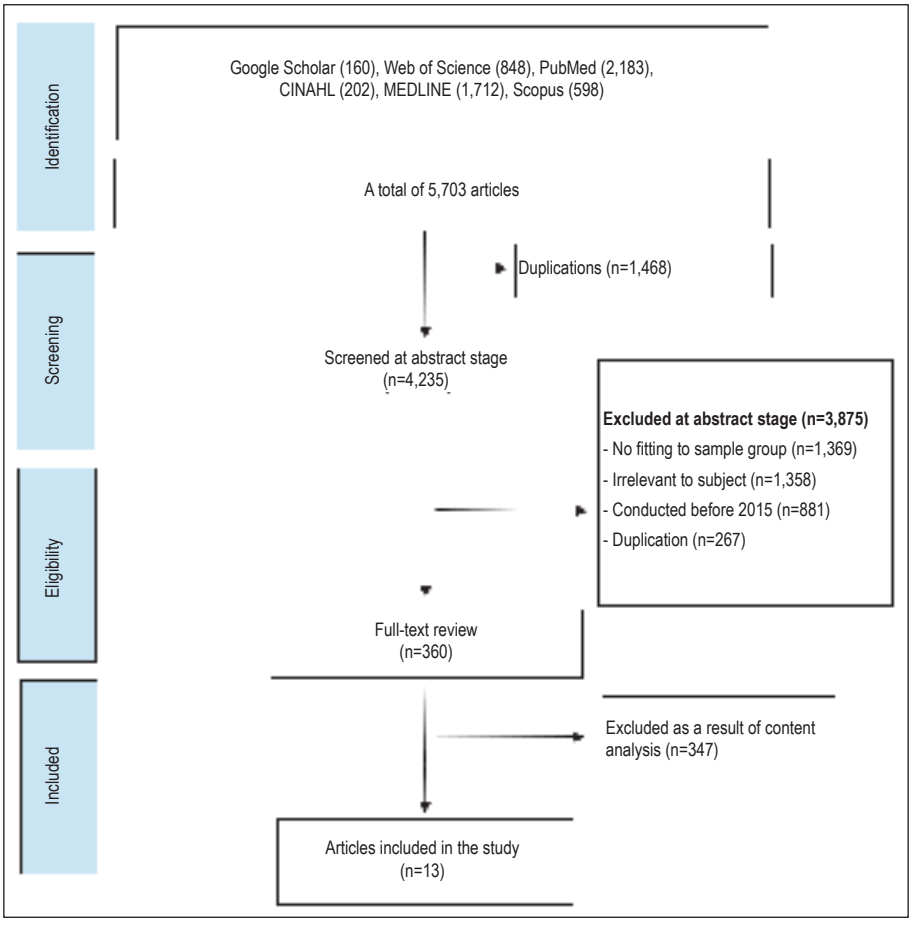

FIGURE 1: PRISMA 2 (Preferred Reporting Items for Systematic Reviews and Meta-analyses Statement).[9]

tween 0.41-0.60 shows a moderate agreement, a kappa agreement rate between 0.61-0.80 shows a high agreement, and a kappa agreement rate above 0.80 shows an excellent agreement.[11]

The odds ratio statistics were used to analyze the effect sizes of the studies. An odds ratio that was greater than one shows that the risk ratio has a positive effect, an odds ratio smaller than one shows that the risk ratio has a negative effect, and an odds ratio equal to 1 shows that it is not effective.[12] The Cochran's Q statistics were used to test the heterogeneity. If the I^2 value determined by the heterogeneity test is below 25%, it was evaluated as no heterogeneity; if it is between 25-50%, it was evaluated as low heterogeneity; if it is between 51-75%, it was evaluated as moderate heterogeneity; and if it is above 75%, it was evaluated as high heterogeneity.[13] The random-effects model was used since the I^2 value was determined as heterogeneous in the parameters examined in the meta-analysis. A value of $p<0.05$ was considered statistically significant.

RESULTS

The meta-analysis of the studies examining adherence to anti-hypertensive treatment in geriatric patients was carried out with 13 studies.

The details of the 13 studies included in the meta-analysis are summarized in Table 1. Four prospective cohort studies, three randomized controlled trials, and six correlational studies were included in the meta-analysis. There were a total of 905,350 patients in the studies. The age of the patients was grouped as over 65 years and under 65 years. The parameters of gender, educational status, income level, place of residence, and presence of comorbid diseases were evaluated.

The scores determined as a result of the quality evaluations of the studies were given in Table 1. The researchers were found to have a high agreement with a value of 0.876 as a result of the kappa test for agreement showing the agreement rates.

EFFECT SIZES AND HETEROGENEITY

Adherence to anti-hypertensive treatment was examined according to six parameters in the meta-analysis. These parameters were age, gender, educational status, income level, place of residence, and presence of comorbid diseases.

As a result of the heterogeneity test for age, gender, educational status, income level, place of residence, and presence of comorbid diseases, the p value was less than 0.05, and Q values were greater than the value corresponding to df value for all. The studies included in the meta-analysis were found to be heterogeneous for all parameters. I^2 values were calculated using the random-effects model, and all values are shown in Table 2.

It was found that adherence to anti-hypertensive treatment decreased with increasing age as a result of the meta-analysis. While all but two of the studies included in the meta-analysis had no significant effect alone, meta-analysis results were found to be significant (Figure 2).

There was no significant effect of gender on adherence to anti-hypertensive treatment. While the effect of the studies was significant alone, the meta-analysis result revealed no significant effect of gender. It was stated that the female gender had a positive effect on adherence to treatment in the studies; gender was found to have no positive or negative effects as a result of the meta-analysis (Figure 3).

Educational status was examined in six of the studies included in the meta-analysis. High educational status was found to have a positive effect on adherence to anti-hypertensive treatment in geriatric patients as a result of the meta-analysis of these six studies (Figure 4).

Income level was examined in eight of the studies included in the meta-analysis. Geriatric patients with high-income levels were found to have high adherence to anti-hypertensive treatment (Figure 5).

Place of residence was examined in six of the studies included in the meta-analysis. It was found that geriatric patients living in the city had higher adherence to treatment, and living in the city had a positive effect on adherence to anti-hypertensive treatment (Figure 6).

TABLE 1: Studies included in the meta-analysis.

Title of the study	Authors of the study	Design of the study	Date of the study	Objective of the study	Parameters examined	Quality Score
Persistence with anti-hypertensives in uncomplicated treatment-naïve very elderly patients: a nationwide population-based study.	Choi et al.[19]	COHORT	2017	To evaluate adherence and persistence to anti-hypertensive medications in treatment.	Age, gender, presence of comorbid diseases, underlying disease, drugs used, type of health insurance.	9.8
Effects of combination drugs on anti-hypertensive medication adherence in a real-world setting: a Korean Nationwide Study.	Kim et al.[20]	COHORT	2019	To determine the effect of combined drugs on adherence to anti-hypertensive medication.	Age, gender, income level, place of residence, type of health insurance, type and number of drugs used.	11.5
Measuring medication adherence in patients with incident hypertension: a retrospective cohort study.	Tang et al.[21]	COHORT	2017	To compare adherence rates by using the methods of receiving concomitant medications.	Age, gender, presence of comorbid diseases, place of residence, income level.	10
Health behaviors and medication adherence in elderly patients	Han et al.[22]	COHORT	2016	To investigate the relationship between health behaviors and medication adherence.	Age, gender, place of residence, type of health insurance, presence of comorbid diseases, smoking status, body mass index, waist circumference, status of alcohol use, physical activity.	8.5
Non-adherence to anti-hypertensive medication: The role of mental and physical comorbidity.	Calderón-Larrañaga et al.[23]	CORRELATIONAL	2016	To investigate the relationship between mental and physical comorbidity and adherence to anti-hypertensive medications in patients attending primary care.	Age, gender, place of residence, blood pressure level, mental and physical comorbidity, polypharmacy, visits to the GP and to physicians with different specialties.	8.5
The association between self-perceptions of aging and anti-hypertensive medication adherence in older Chinese adults.	Hou et al.[24]	CORRELATIONAL	2016	To describe the relationship between aging perceptions and anti-hypertensive medication adherence in elderly adults.	Age, gender, religious belief, place of residence, marital status, income level, type of health insurance, presence of comorbid diseases, blood pressure level, body mass index.	9
The effect of depression on adherence to anti-hypertensive medications in elderly individuals with hypertension.	Demirtürk et al.[25]	CORRELATIONAL	2018	To investigate the effect of depression on adherence to anti-hypertensive medications in patients with hypertension.	Age, gender, educational status, marital status, income level, presence of comorbid diseases, body mass index, blood pressure control.	12
[Compliance with drug treatment in geriatric patients with hypertension].	Özdemir et al.[26]	CORRELATIONAL	2016	To examine medication adherence in geriatric hypertensive patients.	Age, gender, marital status, polypharmacy, presence of comorbid diseases, short form of the Medication Adherence Self-Efficacy Scale.	7.5
Depression and medication adherence among older Korean patients with hypertension: Mediating role of self-efficacy.	Son et al.[27]	CORRELATIONAL	2016	To examine the mediating role of self-efficacy in the relationship between depression and medication adherence in elderly patients with hypertension.	Age, gender, educational status, marital status, working status, income level, daily living activities.	8
Decomposing the effect of drug benefit program on anti-hypertensive medication adherence among the elderly in urban China.	Ma et al.[28]	CORRELATIONAL	2019	To investigate non-adherence between drug benefit program enrollees and non-enrollees and its effect on anti-hypertensive medication.	Age, gender, educational status, income level, place of residence, annual number of check-ups, duration of having hypertension.	8
A successful multifaceted trial to improve hypertension control in primary care: why did it work?	Margolis et al.[29]	RANDOMIZED CONTROLLED	2015	To determine which method is better for controlling hypertension.	Age, gender, educational status, working status, blood pressure level, salt intake score, anti-hypertensive drug class, physical activity, status of alcohol use.	10
Effect of an educational program based on health belief model on medication adherence in elderly patients with hypertension.	Yazdanpanah et al.[30]	RANDOMIZED CONTROLLED	2019	To determine the effect of a Health Belief Model (HBM) based educational program on medication adherence in elderly adults with hypertension.	Age, gender, marital status, educational status, working status, presence of hypertension in the family.	8
Effect of expectation of care on adherence to anti-hypertensive medications among hypertensive blacks: analysis of the Counseling African Americans to Control Hypertension (CAATCH) trial.	Grant et al.[31]	RANDOMIZED CONTROLLED	2016	To investigate the mediating effects of hypertension care, social support, knowledge of hypertension, expectation of medication adherence, adjusting for age.	Age, gender, educational status, income level, presence of health insurance.	10

TABLE 2: Heterogeneity test results according to the parameters.

Heterogeneity test	Q value	df (Q) value	p value	I^2 value
Age	35.186	12	0.000	65.896
Gender	26.450	5	0.000	81.096
Educational status	15.065	5	0.010	66.811
Income level	19.400	7	0.007	63.918
Place of residence	13.817	5	0.017	63.812
Presence of comorbid diseases	35.119	5	0.000	85.763

df: Degree of freedom.

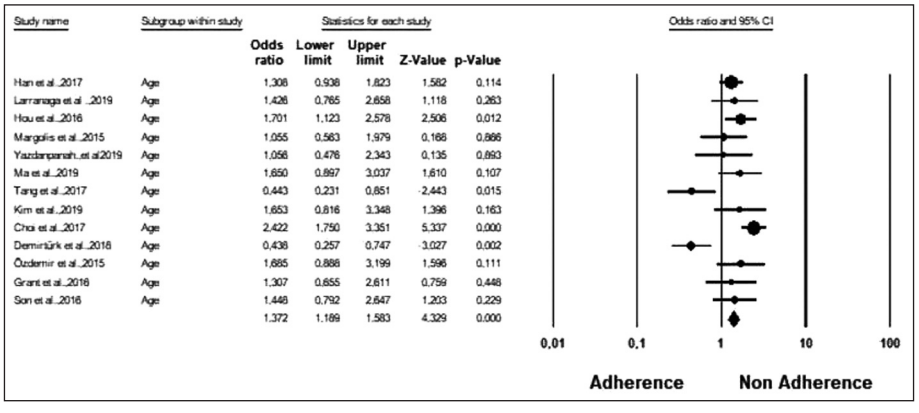

FIGURE 2: Forest plot graph showing the effect of age on adherence to anti-hypertensive treatment.

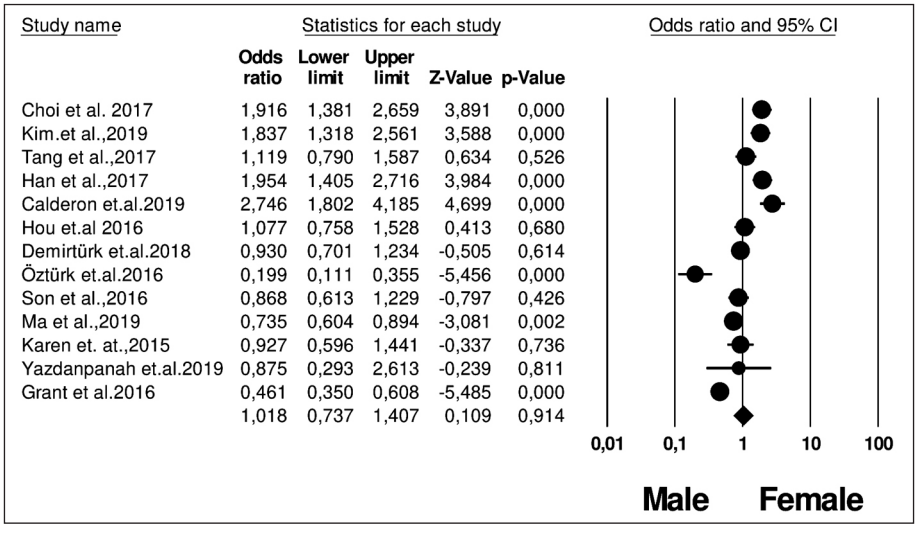

FIGURE 3: Forest plot graph showing the effect of gender on adherence to anti-hypertensive treatment.

The presence of comorbid diseases was examined in six of the studies included in the meta-analysis. It was determined that adherence to anti-hypertensive treatment was adversely affected in geriatric patients with comorbid diseases (Figure 7).

PUBLICATION BIAS ANALYSIS

Whether there was publication bias was determined by the funnel plot (Figure 8) and calculation of Kendall's Tau-b coefficient. That Kendall's Tau-b coefficient was -0.21 and the double-tailed p value was 0.29 showed that there was no publica-

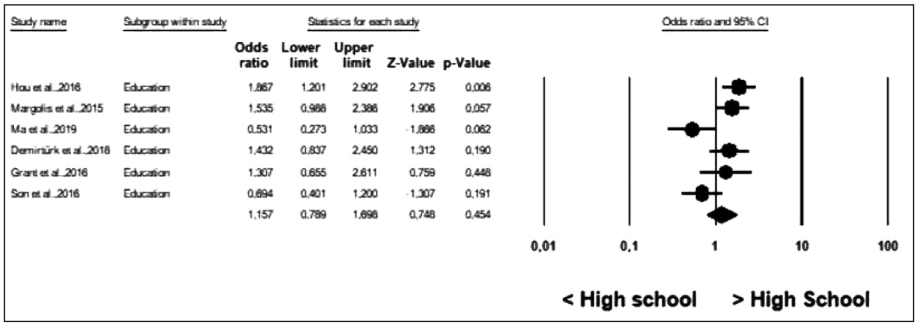

FIGURE 4: Forest plot graph showing the effect of educational status on adherence to anti-hypertensive treatment.

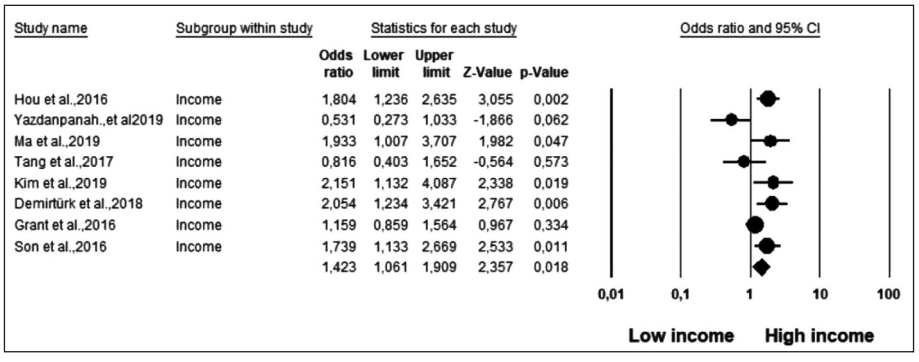

FIGURE 5: Forest plot graph showing the effect of income level on adherence to anti-hypertensive treatment.

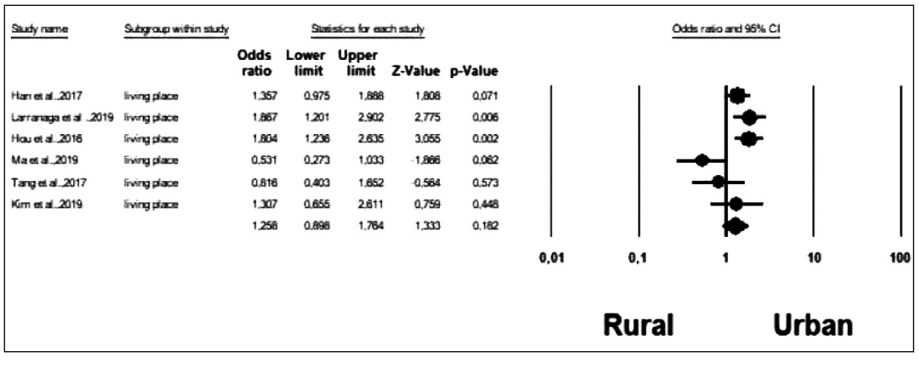

FIGURE 6: Forest plot graph showing the effect of place of residence on adherence to anti-hypertensive treatment.

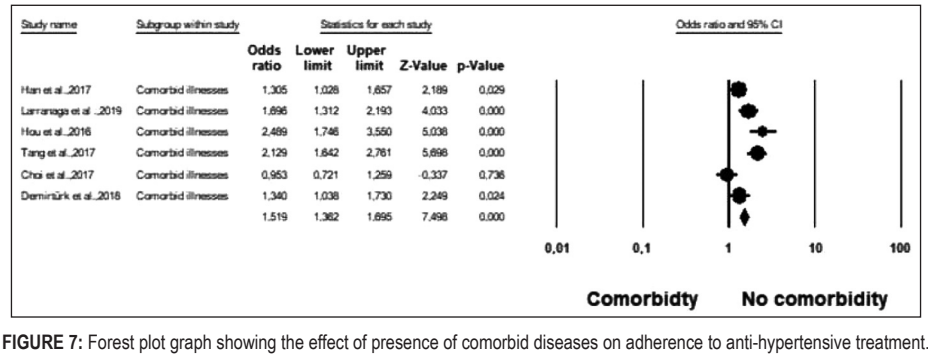

FIGURE 7: Forest plot graph showing the effect of presence of comorbid diseases on adherence to anti-hypertensive treatment.

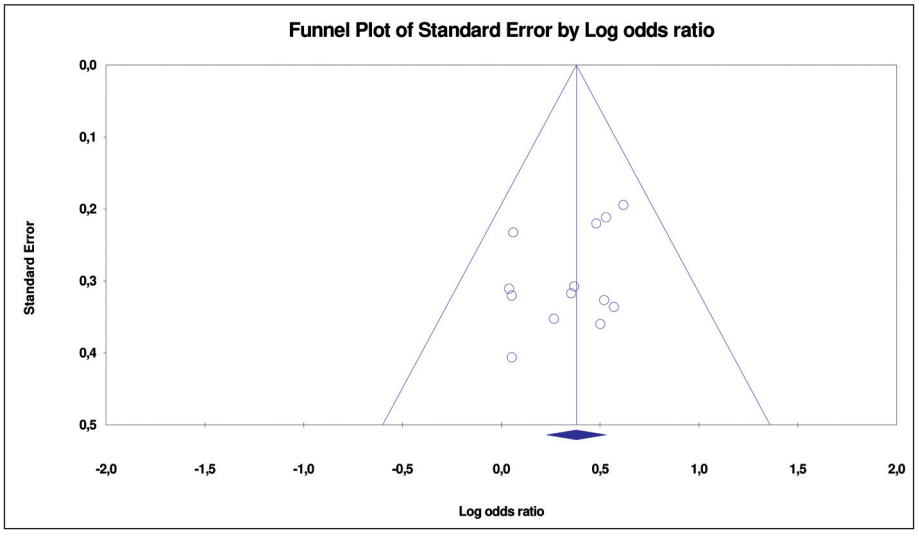

FIGURE 8: Funnel plot.

tion bias in the studies included in the meta-analysis.[14]

DISCUSSION

As a result of the meta-analysis of the studies evaluating adherence to anti-hypertensive treatment in geriatric patients, it was found that some parameters had positive effects, some had negative effects, and some had no effects on adherence to treatment.

According to the literature, the studies revealed various results in terms of the effect of gender on treatment adherence in geriatric patients. One of the studies showed that treatment adherence of the male gender was higher than that of women.[14] Another study examining the effect of male gender on treatment adherence was found to create a negative trend despite not having a statistically significant effect.[15] On the other hand, adherence of the female gender to treatment was observed to be higher than that of men in the studies included in the meta-analysis. However, it was found that gender had no effect on treatment adherence as a result of the meta-analysis. It was thought that this difference was due to insufficient sampling while conducting the studies.

Sertel et al. showed that the cognitive, psychological, and functional status of geriatric individuals were negatively affected with increasing age.[16] It was confirmed by the literature that the decrease in the cognitive, psychological, and functional status of geriatric individuals made treatment adherence processes difficult. As a result of the meta-analysis, it was found that adherence to anti-hypertensive treatment decreased as the age group increased in the patients over 60 years of age, which was similar to the literature. The negative effect of age on adherence to anti-hypertensive treatment was thought to be related to the decrease in the cognitive levels of geriatric patients with increasing age.

It was seen in the literature that the patients with higher educational status had higher adherence to treatment than those with low educational status.[14] The result of the meta-analysis showed similarities with the literature. There may be several reasons for this positive relationship between high educational status and adherence to treatment. One of these may be that they want to have more knowledge of their treatments and believe in the benefits of the treatment. In addition, knowing that they can reduce the risks of cardiovascular disease by adherence to treatment may accelerate the adherence process.

Meta-analysis showed that a high-income level and being a resident of the city positively affected adherence to anti-hypertensive treatment in geriatric patients. The literature shows that income level has a positive effect on the knowledge of medication use.[17] This result was thought to be due to the easy

access to the hospital in the city center. In addition, it was thought that a high-income level had a positive effect on adherence to treatment as it would facilitate patients' demand for treatment and access to medicine.

According to the literature, the increase in the number of medications used per day (3 and above) and the usage of medications other than anti-hypertensive medications were the risk factors for medication errors. Medication errors were seen to increase as the number of medications used for anti-hypertensive treatment and the number of medications used for concomitant diseases increased.[18] It was thought that the use of many different medications would increase the likelihood of medication errors, and these errors would decrease adherence to treatment. The results of the meta-analysis showed similar results with the literature and were confirmed, considering the fact that geriatric patients with comorbid diseases used different medications in addition to anti-hypertensive treatment. Geriatric patients with comorbid diseases were found to have low adherence to anti-hypertensive treatment in the meta-analysis.

CONCLUSION

In conclusion, it was confirmed by the meta-analysis that age and the presence of comorbid diseases decreased adherence to anti-hypertensive treatment in geriatric patients. It was also confirmed by the meta-analysis that being a resident of the city and high educational status and income level increased adherence to anti-hypertensive treatment. In contrast to the literature, it was found that gender did not affect adherence to anti-hypertensive treatment in any way.

Age is an irreversible risk factor that decreases adherence to treatment in geriatric patients. According to this result, it is recommended that geriatric patients should be followed up considering this condition.

It is also recommended to increase the knowledge of the elderly by providing information to them according to their educational status in order to increase adherence to anti-hypertensive treatment in geriatric patients and to facilitate access to hospital and medications for adherence of geriatric patients who do not live in the city.

Comorbid diseases are observed in the majority of geriatric patients. Control and follow-up of comorbid diseases may have a positive effect on treatment. In this context, it is recommended that comorbid diseases such as diabetes and cardiovascular diseases should be followed up more frequently besides hypertension.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and/or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Emine Özdemir Aslan, Fadime Çınar, Fatma Eti Aslan;* ***Design:*** *Emine Özdemir Aslan, Fadime Çınar, Fatma Eti Aslan;* ***Control/Supervision:*** *Fatma Eti Aslan;* ***Data Collection and/or Processing:*** *Emine Özdemir Aslan, Fadime Çınar;* ***Analysis and/or Interpretation:*** *Fadime Çınar, Emine Özdemir Aslan, Fatma Eti Aslan;* ***Literature Review:*** *Emine Özdemir Aslan;* ***Writing the Article:*** *Emine Özdemir Aslan;* ***Critical Review:*** *Fatma Eti Aslan, Fadime Çınar. Thank you to Fadime Çınar, who conducted the English audit and statistical analysis in this study, and Fatma Eti Aslan for evaluating the scientific content.*

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