

Research Article | Araştırma Makalesi

RELATIONSHIP BETWEEN ERECTILE DYSFUNCTION AND ASYMMETRIC DIMETHYL ARGININE LEVELS IN PATIENTS WITH END-STAGE RENAL DISEASE

SON DÖNEM BÖBREK HASTALIĞI OLAN HASTALARDA EREKTİL DİSFONKSİYON VE ASİMETRİK DİMETİL ARGİNİN DÜZEYLERİ ARASINDAKİ İLİŞKİ

 Burak Can¹  Sibel Gökçay Bek^{2*},  Metin Ergül²,  Adnan Batman³  Necmi Eren²  Ramazan Azim Okyay⁴  Betül Kalender²  Erkan Dervişoğlu²

¹Acıbadem Hospital, Department of Internal Medicine, Adana, Türkiye. ²Kocaeli University, Faculty of Medicine, Department of Nephrology, Kocaeli, Türkiye. ³Koç University Hospital, Department of Endocrinology, Istanbul, Türkiye. ⁴Kahramanmaraş Sütçü İmam University, Department of Public Health, Kahramanmaraş, Türkiye



ABSTRACT

Objective: Asymmetric dimethylarginine is a major inhibitor of nitric oxide synthesis. Erectile dysfunction and chronic kidney disease (CKD) are associated with elevated levels of asymmetric dimethylarginine. This study aimed to examine the effects of ADMA on erectile dysfunction in patients undergoing peritoneal hemodialysis.

Methods: A total of 32 peritoneal, 32 hemodialysis patients, and 32 healthy male volunteers were included in the study. Serum asymmetric dimethylarginine levels were measured, and clinical and laboratory parameters were analyzed. The International Index of Erectile Function-5 was used to evaluate sexual function and the Pittsburgh Sleep Quality Index was used to evaluate sleep quality. Depressive symptoms were assessed using the Beck depression inventory.

Results: Asymmetric dimethylarginine levels differed significantly among the three groups ($p < 0.001$). It was higher in patients undergoing hemodialysis than in those undergoing peritoneal dialysis ($p < 0.002$). Erectile dysfunction was detected more frequently in the patient group than in the control group ($p < 0.001$). However, correlation analysis revealed no significant relationship between asymmetric dimethylarginine levels and erectile dysfunction scores. There was a negative correlation between the erectile dysfunction score, sleep quality, and depression scale scores. Asymmetric dimethylarginine showed a significant positive correlation with treatment duration, phosphorus, calcium-phosphorus product, and parathormone. A negative correlation was observed between albumin, cholesterol, low-density lipoprotein (LDL), residual urine, and asymmetric dimethylarginine levels. Residual urine amount in the correlation analysis showed a negative correlation with asymmetric dimethylarginine, phosphorus, and calcium-phosphorus products and a positive correlation with total cholesterol and low-density lipoprotein.

Conclusion: Residual renal function and urine amount are important parameters that correlate with ADMA levels for sustainable healthy erectile function in CKD.

Keywords: ADMA, Erectile Dysfunction

Öz

Amaç: Asimetrik dimetilarginin, nitrik oksit sentezinin majör inhibitörüdür. Erektile disfonksiyon ve kronik böbrek hastalığı (KBH), yüksek asimetrik dimetilarginin seviyeleriyle ilişkili bulunmuştur. Bu çalışma, ADMA'nın peritoneal hemodiyaliz geçiren hastalarda erektile disfonksiyon üzerindeki etkilerini incelemeyi amaçlamıştır.

Yöntem: Çalışmaya toplam 32 peritoneal, 32 hemodiyaliz hastası ve 32 sağlıklı erkek gönüllü dahil edildi. Serum asimetrik dimetilarginin seviyeleri ölçüldü ve klinik ve laboratuvar parametreleri analiz edildi. Cinsel fonksiyonu değerlendirmek için Uluslararası Erektile Fonksiyon İndeksi-5 ve uyku kalitesini değerlendirmek için Pittsburgh Uyku Kalitesi İndeksi kullanıldı. Depresif semptomlar Beck Depresyon Envanteri Ölçeği kullanılarak değerlendirildi.

Bulgular: Asimetrik dimetilarginin seviyeleri üç grup arasında önemli ölçüde farklılık gösterdi ($p < 0,001$). Hemodiyalize giren hastalarda peritoneal diyalizi yapanlara göre daha yüksekti ($p < 0,002$). Hasta grubunda erektile disfonksiyon kontrol grubuna göre daha sık tespit edildi ($p < 0,001$). Ancak korelasyon analizi asimetrik dimetilarginin düzeyleri ile erektile disfonksiyon skorları arasında anlamlı bir ilişki olmadığını ortaya koydu. Erektile disfonksiyon skoru, uyku kalitesi ve depresyon ölçeği skorları arasında negatif korelasyon gösterdi. Asimetrik dimetilarginin tedavi süresi, fosfor, kalsiyum-fosfor ürünü ve parathormon ile anlamlı pozitif korelasyon gösterdi. Albümin, kolesterol, düşük yoğunluklu lipoprotein (LDL), rezidüel idrar ve asimetrik dimetilarginin düzeyleri arasında negatif korelasyon gözlemlendi. Korelasyon analizindeki rezidüel idrar miktarı asimetrik dimetilarginin, fosfor ve kalsiyum-fosfor ürünleri ile negatif korelasyon, toplam kolesterol ve düşük yoğunluklu lipoprotein ile pozitif korelasyon gösterdi.

Sonuç: Kronik böbrek hastalığında (KBH) sürdürülebilir sağlıklı erektile fonksiyon için rezidüel böbrek fonksiyonu ve idrar miktarı, ADMA düzeyleriyle korelasyon gösteren önemli parametrelerdir.

Anahtar Kelimeler: ADMA, Erektile Disfonksiyon

Introduction

Asymmetric dimethylarginine (ADMA) is a significant inhibitor of endothelial nitric oxide synthase (eNOS) production and L-arginine entry into cells.¹ ADMA has been discovered to significantly increase the uncoupling of eNOS and generate free radicals.^{2,3}

Recent studies have demonstrated that ADMA plays a crucial role in predicting the likelihood of cardiovascular complications and death in individuals with chronic kidney disease (CKD) who are either pre-dialysis or dialysis-dependent.^{4,5} ADMA causes vasoconstriction and inhibition of acetylcholine-induced vasorelaxation in the brain.⁶ This plays a significant role in the cognitive decline in patients with CKD. ADMA has also been linked to the development of many comorbidities affecting whole human physiology.⁷⁻¹⁴ Studies have connected ADMA to the activation of polymorphonuclear cells and expression of adhesion molecules.¹⁵

Erectile dysfunction (ED) is a common problem in patients with CKD and its frequency increases in patients undergoing dialysis.¹⁶ Mental disorders, drug side effects, decreased penile vascularity, and hormonal factors are associated with its etiology.¹⁷

Nonetheless, there is a lack of randomized clinical research examining the possible impact of arginine on erectile function in patients with CKD. This research sought to explore the connection between ADMA and erectile dysfunction in individuals receiving dialysis treatment.

Methods

This study included patients receiving dialysis treatment at the Kocaeli University Faculty of Medicine Hospital. The inclusion criteria were as follows: age > 18 years, male sex, married or having a sexual partner, having undergone peritoneal dialysis (PD)/hemodialysis (HD) for at least three months, and volunteering to participate in the study. The exclusion criteria were female sex, diabetes mellitus, psychiatric disorders, active infection, alcohol and substance addiction, malignancy, serious neurological diseases, and cardiac and hepatic failure. Age, marital status, and routine habits were recorded by meeting the patients one-on-one. The International Index of Erectile Function-5 (IIEF-5), Pittsburgh Sleep Quality Index (PSQI), and Beck Depression Inventory (BDI) were used to evaluate erectile function, sleep quality, and depressive symptoms, respectively. Blood samples were collected from patients undergoing HD and peritoneal dialysis to determine ADMA levels. Blood was obtained from patients undergoing hemodialysis prior to dialysis and peritoneal exchange.

Information such as the dialysis duration, body mass index, the underlying cause of end-stage kidney disease (ESKD), type of peritoneal dialysis (PD), frequency of daily exchanges, daily ultrafiltration for hemodialysis (HD) patients, weekly duration and frequency of hemodialysis,

dry weight, and the volume of ultrafiltration was extracted from the medical records.

Urea, creatinine, sodium, potassium, phosphorus, calcium, alkaline phosphatase, total protein, albumin, hemoglobin, sedimentation, C-reactive protein (CRP), parathyroid hormone (PTH), iron, transferrin saturation, ferritin, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), serum triglyceride (TG), uric acid, hemoglobin, mean platelet volume (MPV), platelets, FSH, LH, total testosterone, residual renal function, and weekly Kt/V values are listed in the files. For patients undergoing hemodialysis, the average Kt/V values in the last 3 months were recorded. After collecting blood samples for ADMA measurement, the serum was stored at 80°C. The Immune Diagnostic ADMA Xpress ELISA Kit (Bendheim, Germany) was used for the ADMA measurements.

Statistical Analysis

Statistical analyses were performed using SPSS 20 for Windows (SPSS Inc., Chicago, IL, USA). Made using the latest version. To evaluate the significance level of the differences between groups, a t-test was used between the two groups, and one-way ANOVA was used between the three groups for normally distributed variables. For variables that were not normally distributed, the Mann–Whitney U test was applied between two groups, and the Kruskal–Wallis test was applied between three groups.

To evaluate the relationship between ADMA and the clinical, biochemical, and quality of life scales, the Pearson correlation test was used for normally distributed variables, and the Spearman correlation test was used for normally distributed variables. Statistical significance was set at $p < 0.05$.

Results

Ninety-six male participants, including 32 patients undergoing HD, 32 undergoing PD, and 32 healthy volunteers, were included in the study. All patients undergoing PD exchanged 2000 ml four times a day. All HD patients underwent dialysis for three days-four hours per week. The mean age was 48.6 ± 11.3 in PD patients, 48.8 ± 12.1 in HD patients, and 46.6 ± 7.4 in the control group. The causes of ESKD in patients undergoing PD included hypertension in 19, glomerulonephritis in two, idiopathic in three, polycystic kidney disease in six, vesicoureteral reflux in one, and nephrolithiasis in one. The causes of ESKD in patients undergoing HD were hypertension in 14 (of patient had both hypertension and polycystic kidney disease), glomerulonephritis in 2, polycystic kidney disease in 5, amyloidosis in 1, idiopathic in 7, congenital renal hypoplasia in 1, nephrolithiasis in 2, and vesicoureteral reflux in 1. In the group of patients receiving hemodialysis, 27 individuals (84.37%) were diagnosed with erectile dysfunction. Comparatively, 20 patients (62.5%) in the peritoneal dialysis category and 8 individuals (25%) in the control group were also affected. Overall, 73.43% of those undergoing dialysis (both HD and PD) experienced erectile dysfunction.

Asymmetric dimethylarginine levels were measured in PD patients: 0.74 ± 0.42 micromol/L, in HD patients: 1.1 ± 0.4 micromol/L, and in the control group: 0.47 ± 0.2 micromol/L. The PSQI, BDI, and IIEF-5 values of PD, HD patients, and the control group, as well as treatment duration, residual urine amount, Kt/V values, and other laboratory data of PD and HD patients, are shown in Table 1. Upon examining the data, it was discovered that there were statistically significant discrepancies in the ADMA, BDI, PSQI, IIEF, and total testosterone levels (Table 1).

A pairwise comparison was performed between the groups to determine the group that had differences in ADMA level, IIEF-5, PSQI, and BDI scores. Bonferroni correction was used, and a p-value <0.0167 was considered significant. (Table 2)

When patients with PD and those with HD were compared, no significant difference was observed between the two groups in terms of IIEF-5, PSQI, BDI scores, and total testosterone levels. ADMA levels were significantly lower in patients undergoing PD than in HD

patients [0.7 ± 0.4 micromol/L, respectively; 1.1 ± 0.4 micromol/L ($p=0.002$)]. In patients with PD, ADMA levels and PSQI scores were higher than those in the control group ($p=0.002$, $p=0.008$, respectively), and the IIEF score was significantly lower ($p<0.0001$). In patients undergoing HD, the IIEF-5 scores were lower ($p<0.001$) and the ADMA, BDI, and PSQI scores were higher than those in the control group (ADMA, $p=0.002$; PSQI, $p=0.002$; BDI, $p<0.0001$).

When the relationships between the laboratory values of HD patients and PSQI, IIEF-5, BDI scores, and ADMA were examined, a significant relationship was found between transferrin and ADMA levels. When peritoneal dialysis and HD patients were taken together as a patient group and the relationship between laboratory values, PSQI, IIEF-5, BDI scores, and ADMA were examined, a significant relationship was found in the same direction with treatment duration, phosphorus, parathormone, MPV, and ferritin, and a significant reverse relationship was found between residual urine amount and LDL.

Table 1. Comparison of variables in peritoneal dialysis and hemodialysis patient groups

	PD patients Mean $\pm$ SD	HD patients Mean $\pm$ SD	p value
Age (year)	48.6 $\pm$ 11.3	48.8 $\pm$ 12.1	0.945
Number of offspring	0.7 $\pm$ 0.4	1.1 $\pm$ 0.4	0.0002
IIEF-5	14.9 $\pm$ 6.9	14.69 $\pm$ 6.8	0.907
ADMA (μ mol/L)	0.7 $\pm$ 0.4	1.1 $\pm$ 0.4	0.0002
PSQI	6.3 $\pm$ 4.1	7.4 $\pm$ 4.7	0.322
BDI	12.0 $\pm$ 10	16.8 $\pm$ 11.5	0.079
Total Testosterone (ng/dL)	357.5 $\pm$ 103.1	263 $\pm$ 124.8	0.001
Duration of Dialysis (months)	52 $\pm$ 34.7	106.1 $\pm$ 67.9	0.0002
Residual Urine (mL)	827.2 $\pm$ 744.3	212.5 $\pm$ 421.8	0.0001
UF Volume(mL)	1339.8 $\pm$ 692.6	3064.1 $\pm$ 992.2	0.0001
Kt/V	2.10 $\pm$ 0.9	1.4 $\pm$ 0.2	0.0001
T. protein (g/dL)	6.2 $\pm$ 0.8	6.7 $\pm$ 0.6	0.006
Albumin (g/dL)	3.5 $\pm$ 0.5	3.8 $\pm$ 0.3	0.005
Calcium (mg/dL)	9.0 $\pm$ 0.7	8.9 $\pm$ 0.9	0.621
Phosphorus (mg/dL)	5.1 $\pm$ 1.3	5.7 $\pm$ 1.6	0.104
Ca – P Product	46.4 $\pm$ 13	50.7 $\pm$ 13.6	0.200
PTH (pg/mL)	603.5 $\pm$ 662.4 (Median: 574.28)	683.4 $\pm$ 468.7 (Median:727.130)	0.579
Total cholesterol (mg/dL)	169.9 $\pm$ 43.3	154.6 $\pm$ 35	0.125
LDL (mg/dL)	107.6 $\pm$ 34.9	80 $\pm$ 30.3	0.001
BMI (kg/m ²)	26.4 $\pm$ 3.8	24.4 $\pm$ 3.5	0.032
Hemoglobin (g/dL)	11.5 $\pm$ 2.2	12.2 $\pm$ 2	0.187
MPV (fL)	7.3 $\pm$ 1.1	8.8 $\pm$ 1	0.0001
Platelet (cells/mm ³)	254.281 $\pm$ 71.026	200.312 $\pm$ 68.263	0.002
Iron (mcg/dL)	72.9 $\pm$ 30	66.9 $\pm$ 48.8	0.555
Transferrin saturation (%)	34.9 $\pm$ 20.9	46.8 $\pm$ 69.1	0.354
Ferritin (ng/mL)	341.5 $\pm$ 280.5 (Median:361.68)	791.6 $\pm$ 956 (Median:833.33)	0.013
Uric Acid (mg/dL)	5.7 $\pm$ 1	6 $\pm$ 1.7	0.392
CRP (mg/L)	1.2 $\pm$ 1.5	1.7 $\pm$ 2	0.262

Abbreviations: SD: Standard deviation, CRP: C-reactive protein, PTH: Parathormone, BMI: Body Mass Index, LDL: Low Density Lipoprotein, MPV: Mean Platelet Volume, UF: Ultrafiltration, ADMA: Asymmetric dimethylarginine, IIEF -5: International Index of erectile Function-5, PSQI: Pittsburgh Sleep Quality Index, BDI: Beck depression Inventory. T-test was used.

Table 2. Comparison of Common Variables Between Groups

	PD (n=32)	HD (n=32)	Control (n=32)	p
	Mean ± SD	Mean ± SD	Mean ± SD	
Age**	48.6 ± 11.3	48.8 ± 12.1	46.6 ± 7.4	0.645
Total Testosterone **(ng/dL)	357.5 ± 103.1	263 ± 124.8	321.4 ± 112.5	0.005
	Median (IQR)	Median (IQR)	Median (IQR)	
ADMA *(µmol/L)	0.7 (0.4)	1.1 (0.4)	0.5 (0.2)	< 0.0001
PSQI *	6.3 (4.1)	7.4 (4,7)	4 (3.1)	0.003
BDI *	12 (10)	16.8 (11.5)	6.7 (4.3)	< 0.0001
IIEF-5 *	14.9 (6.9)	14.7 (6.8)	22.3 (2.8)	< 0.0001

Abbreviations: SD: Standard deviation, IQR: Interquartile range ADMA: Asymmetric dimethylarginine, IIEF -5: International Index of erectile Function-5, PSQI: Pittsburgh Sleep Quality Index, BDI: Beck depression Inventory. *Kruskal Wallis, **One Way ANOVA

Table 3. Association between ADMA levels and other variables in HD and PD groups.

	r	p
Age ^b	0.008	0.947
IIEF-5 ^b	0.068	0.595
PSQI ^b	0.006	0.961
Total testosterone ^a	-0.200	0.114
Treatment period ^b	0.251	0.046
Residual urine volume ^b	-0.413	0.001
Total protein ^b	-0.138	0.276
Albumin ^b	-0.260	0.038
Calcium ^b	-0.187	0.150
Phosphorus ^a	0.296	0.018
Calcium x phosphorus product ^b	0.217	0.086
Parathormone ^b	0.451	0.0001
Total cholesterol ^b	-0.229	0.069
HDL ^b	-0.234	0.062
LDL ^b	-0.250	0.047
Hemoglobin ^b	-0.017	0.892
Transferrin saturation ^b	0.059	0.642
Ferritin ^b	0.276	0.027
Uric acid ^a	0.114	0.368
CRP ^b	0.214	0.089

Abbreviations: ADMA: Asymmetric dimethylarginine, IIEF-5: International Index of Erectile Function-5, PSQI: Pittsburgh Sleep Quality Index, BDI: Beck Depression Inventory, CRP: C-reactive protein, LDL: Low Density Lipoprotein, HDL: High Density Lipoprotein

^a Pearson correlation analysis, ^b Spearman correlation analysis

Table 4. Residual urine volume and variables associated with residual urine volume

	Residual urine volume
ADMA	-0.413**
Total testosterone	0.413**
Total cholesterol	0.249*
LDL	0.336**
Phosphorus	-0.402**
Parathormone	-0.329**
Calcium x Phosphorus Product	-0.397**

Spearman correlation test was used. * p<0.05, ** p<0.01

ADMA: Asymmetric dimethylarginine, LDL: Low Density Lipoprotein

Discussion

The ADMA levels were higher in the ESKD group than in the control group. Furthermore, patients undergoing HD had significantly higher ADMA levels than those undergoing PD. The results of this study are consistent with those of previous studies. A study by Zhang et al.¹⁸ in 2010 revealed that ADMA levels were at their lowest in healthy individuals, increased in patients undergoing PD, and reached their peak in those receiving HD. ADMA is linked to an increased risk of cardiovascular issues. In patients with ESKD, the removal of high ADMA content from the body may decrease the risk of morbidity and mortality.¹⁹ In some instances, choosing peritoneal dialysis could offer greater benefits in potentially

lowering mortality rates when compared to hemodialysis.

After evaluating patients with PD and HD individually, no correlation was observed between ADMA and IIEF-5 scores. The outcomes remained consistent when the PD and HD patients were combined into a single group. Erectile dysfunction in individuals with ESKD can occur for several reasons in addition to an increase in ADMA levels, which impedes nitric oxide synthesis. Paroni et al.²⁰ examined patients who were exclusively monitored in the ED. The findings revealed that both arteriogenic and non-arteriogenic ED patients exhibited higher levels of ADMA than the control subjects. ADMA levels were higher in patients with arteriogenic ED than in those without. Due to the limitations of performing penile Doppler on patients who participated in the study, it was not feasible to differentiate between arteriogenic and non-arteriogenic ED. As a result, no remarks were made regarding the relationship between IIEF score and ADMA in patients undergoing dialysis with either type of ED.

Studies have indicated that people with ED often exhibit a higher mean platelet volume, which indicates heightened platelet activity. This points to a likelihood of platelet aggregation, regardless of the root cause.²¹ In this study, a connection was observed between ADMA and MPV levels. Previous studies have not documented this association or the impact of MPV on patients with CKD.^{22,23,24}

IIEF scores were significantly lower in patients with PD and HD than in the control group, and erectile dysfunction, depression, and sleep disorders were more common in patients with ESKD than in the normal population.²⁵ When patients undergoing PD and HD were compared, no significant differences in the IIEF-5, BDI, and PSQI scores were observed. Erectile dysfunction is common in dialysis patients. Patients express sleep-related and psychological distress, but have difficulty expressing complaints about sexual dysfunction. This situation also caused difficulties in filling out the questionnaires and in daily practice. Quality of life variables and sexual dysfunction experienced by patients undergoing physical examination and laboratory tests should be thoroughly assessed, particularly those that are difficult to articulate. In this study, the incidence of depression was higher in the patient group than in the nonpatient group.

The frequency of erectile dysfunction in patients with chronic kidney disease is approximately 20%–87.7%.^{26,27,28} The frequency of ED among patients included in the study was 68.8% in the PD group and 81.3% in the HD group. ED was more common in patients undergoing HD than in those undergoing PD; however, this difference was not statistically significant.

Several factors can cause ED in ESKD patients. Factors such as vascular problems, medications, hormonal changes, psychological stress, zinc deficiency, and anemia play a role in the development of erectile dysfunction.²⁸ In the analysis we conducted to determine the factors affecting the IIEF-5 score of the patient group, there was a negative correlation between the amount of

residual urine, PSQI and BDI scores, and the IIEF score. In addition, age correlated with erectile dysfunction. No relationship was found between other laboratory markers and IIEF-5 in the hemodialysis group.

In the peritoneal dialysis group, there was a significant inverse relationship between ADMA and total protein and albumin levels, which are nutritional markers.²⁹ When the PD and HD groups were considered together, no significant relationship was found with total protein, whereas a significant negative correlation was found between albumin and ADMA levels. Many studies have shown a negative correlation between plasma albumin concentration and a positive correlation between high ferritin levels and morbidity in patients undergoing PD or HD.³⁰ Given that both are significant indicators of inflammation, it makes sense to comprehend this connection.

When we examined the relationship between total cholesterol, LDL, and ADMA in our patients, we found a negative correlation. The negative correlation between total cholesterol and LDL, which increases the risk of atherosclerosis in the normal population, and ADMA, which increases vascular endothelial damage in patients with ESKD, is consistent with previous studies and once again reveals the importance of nutritional status in patients undergoing dialysis.^{31,32} Hypocholesterolemia is a strong risk factor for mortality in patients undergoing dialysis and a marker of poor nutritional status.³³ Similar to hypoalbuminemia, hypocholesterolemia is thought to be associated with inflammation.

In this study, ADMA was significantly associated with inorganic phosphorus and PTH levels. ADMA is a predictive marker of hyperparathyroidism.³⁴ Although it cannot be concluded that ADMA causes PTH secretion, an increase in ADMA and PTH values occurs together.³⁵ No significant relationship was found between ADMA and calcium and phosphorus levels, which are other factors contributing to vascular calcification in this study, probably due to the small number of patients.

The most significant data in this study were related to the amount of residual urine volume. A significant negative correlation was found between residual urine function and ADMA, phosphorus, PTH, calcium phosphorus product values, and treatment duration, whereas a positive correlation was found between total cholesterol, LDL, and total testosterone levels. A notable correlation between ADMA and total testosterone levels has been observed in patients with hypogonadotropic conditions.^{36,37} However, this association has not been documented in patients with CKD.

Residual renal function is an important predictor of survival in patients.^{36,37} Very few large-scale studies have been conducted on patients undergoing hemodialysis. The CHOICE study showed that mortality was reduced in patients undergoing hemodialysis with residual renal function, regardless of the cause.³⁸ Many studies have shown that patients with residual renal function have better nutritional status than those without residual renal function.³⁹ Emphasizing the preservation of the remaining kidney's function may play a crucial role in

enhancing patients' overall quality of life and sexual health.⁴⁰

Conclusion

In conclusion, this study confirmed the elevated ADMA levels in dialysis patients, which vary based on the type of dialysis they undergo. Although a direct relationship between ADMA and ED was not found, its associations with nutritional markers, mineral metabolism, and especially the impact of residual renal function on various biochemical parameters, underscore the importance of a multidimensional approach in managing this patient population. Future studies should be conducted in larger patient cohorts to understand better the role of ADMA in the pathophysiology of CKD and to evaluate the long-term effects of different dialysis modalities.

Ethical Approval

The study complied with the Declaration of Helsinki. Ethical approval for the study was obtained from the ethics committee of Kocaeli University Hospital (GOKAEK-KOU KAEK 2014/42). Informed consent was obtained from all the participants when they were enrolled.

Conflict of Interest

The authors declare no conflicts of interest.

Author Contributions

BC, ED: Concept-Design; BC, ME, NE, SGB, AB: Data curation; BC, SGB, ED, RAO: Formal Analysis; NA: Funding acquisition; BC, ME, AB: Investigation; BC, ED: Methodology; ED: Project administration; BC, ME, NE, RAO, AB: Resources; ED, SGB, BK: Supervision; BC, SGB: Validation; BC: Visualization; BC, SGB, ED: Writing – original draft; BC, SGB, ED, BK: Writing – review & editing.

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