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Infection

A multicenter study of the clinical, laboratory characteristics, and potential prognostic factors in patients with amyloid A amyloidosis on hemodialysis

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Abstract

Introduction: While light chain (AL) amyloidosis is more common in western countries, the most common type of amyloidosis is amyloid A (AA) amyloidosis in Eastern Mediterranean Region, including Turkey. Although worse prognosis has been attributed to the AL amyloidosis, AA amyloidosis can be related to higher mortality under renal replacement therapies. However, there are no sufficient data regarding etiology, clinical presentation, and prognostic factors of AA amyloidosis. The objective of our study is to evaluate the clinical, laboratory characteristics, and possible predictive factors related to mortality in patients with AA amyloidosis undergoing hemodialysis (HD).

Methods: This multicenter, cross-sectional study was a retrospective analysis of 2100 patients on HD. It was carried out in 14 selected HD centers throughout Turkey. Thirty-two patients with biopsy-proven AA amyloidosis and thirty-two control patients without AA amyloidosis undergoing HD were included between October 2018 and October 2019. There was no significant difference between the groups in terms of age and dialysis vintage. Causes of AA amyloidosis, treatment (colchicine and/or anti-interleukin 1 [IL] treatment), and the number of familial Mediterranean fever (FMF) attacks in the last year in case of FMF, systolic and diastolic blood pressures, biochemical values such as mean CRP, hemoglobin, serum albumin, phosphorus, calcium, PTH, ferritin, transferrin saturation, total cholesterol levels, EPO dose, erythropoietin-stimulating agents resistance index, interdialytic fluid intake, body mass indexes, heparin dosage, UF volume, and Kt/V data in the last year were collected by retrospective review of medical records.

Findings: Prevalence of AA amyloidosis was found to be 1.87% in HD centers. In amyloidosis and control groups, 56% and 53% were male, mean age was 54 ± 11 and 53 ± 11 years, and mean dialysis vintage was 104 ± 94 and 107 ± 95 months, respectively. FMF was the most common cause of AA

Abbreviations: AA, amyloid A; AL, amyloid light chain; AS, ankylosing spondylitis; CRP, C-reactive protein; DBP, diastolic blood pressure; DPO, darbepoetin; EPO, erythropoietin; ESRD, end-stage renal disease; FMF, familial Mediterranean fever; HD, hemodialysis; Hgb, hemoglobin; IBD, inflammatory bowel disease; IL, interleukin; JIA, juvenile idiopathic arthritis; MICS, malnutrition-inflammation complex syndrome; PTH, parathyroid hormone; RA, rheumatoid arthritis; SAID, systemic autoinflammatory disease; SBP, systolic blood pressure; UF, ultrafiltration.

amyloidosis (59.5%). All FMF patients received colchicine and the mean colchicine dose was 0.70 ± 0.30 mg/day. 26.3% of FMF patients were unresponsive to colchicine and anti-IL-1 treatment was used in these patients. In AA amyloid and control groups, erythropoietin-stimulating agents resistance index were 7.88 ± 3.78 and 5.41 ± 3.06 IU/kg/week/g/dl, respectively ($p = 0.008$). Additionally, higher CRP values (18.78 ± 18.74 and 10.61 ± 10.47 mg/L, $p = 0.037$), lower phosphorus (4.68 ± 0.73 vs. 5.25 ± 1.04 mg/dl, $p = 0.014$), total cholesterol (135 ± 42 vs. 174 ± 39 mg/dl, $p < 0.01$), and serum albumin (3.67 ± 0.49 mg/dl, 4.03 ± 0.22, $p < 0.01$) were observed in patients with AA amyloidosis compared to the control group.

Discussion: In this study, we found that long-term prognostic factors including higher inflammation, malnutritional parameters, and higher erythropoietin-stimulating agents resistance index were more frequent in AA amyloidosis patients under HD treatment.

KEYWORDS
AA amyloidosis, end-stage renal disease, etiology, familial Mediterranean fever, hemodialysis, inflammation, renal amyloidosis

INTRODUCTION

Amyloidoses are characterized by the presence of extracellular amyloid deposits, consisting of fibrillar aggregates of misfolded β-sheet proteins.[1] The global incidence of amyloidosis is estimated at five to nine cases per million patient-years.[2] More than 25 structurally unrelated proteins have been identified to cause amyloidosis in humans.[3] The main subtypes of systemic amyloidosis are primary AL (amyloid light chain) amyloidosis, secondary amyloid A (AA) amyloidosis, familial amyloidosis, and ß2-microglobulin-related amyloidosis.[4] AA amyloidosis is the most common type of amyloidosis in the Eastern Mediterranean Region including Turkey[5] and is associated with underlying infections and chronic inflammatory diseases. On the other hand, systemic AL amyloidosis that was known as primary amyloidosis; is the most prevalent type in developed countries.[6] In the last few decades, AL amyloidosis is an increasingly diagnosed disorder in developed countries; whereas the incidence of AA amyloidosis has considerably decreased thanks to new therapeutic strategies in chronic infectious and inflammatory diseases.[7] In AL amyloidosis, while the prognosis mostly depends on kidney involvement, cardiac involvement, as well as response to the treatment including chemotherapy and/or allogeneic bone marrow transplantation.[8] However, there is a paucity of information regarding prognosis in AA amyloidosis which can be developed from very heterogeneous diseases with chronic inflammatory status, including; familial Mediterranean fever,

chronic osteomyelitis, inflammatory bowel diseases, Behcet's disease, rheumatoid arthritis, drug use with skin popping, and tuberculosis.[9]

The kidney is a frequent site of amyloid deposition in most types of systemic amyloidosis, especially in AL, AA, fibrinogen, lysozyme, apoAII, and, to a lesser extent, apoAI disease. Most studies have demonstrated that the kidney is affected 50%–80% in individuals with AL amyloidosis.[10–12] Proteinuria (composed mainly of albumin, with detectable urine monoclonal immunoglobulin light chain) and decreased glomerular filtration rate, which are present in 20%–45% of patients with AL amyloidosis are the cardinal presenting clinical features.[11] About 19% of cases of AL amyloidosis will require renal replacement therapy (RRT) during the course of their disease.[13] On the contrary, there are scant data evaluating the renal involvement in AA amyloidosis which typically manifests with proteinuria, nephrotic syndrome, and, often progression to end-stage renal disease (ESRD) if insufficiently treated chronic inflammatory state.[14,15] At the time of diagnosis, 11% of the patients with AA amyloidosis had an end-stage renal failure[16] and approximately half (56.2%) of these patients ultimately receive renal replacement therapy during long-term follow-up.[17] After the development of ESRD, AA amyloid patients can be treated with renal replacement therapies including hemodialysis, peritoneal dialysis, and kidney transplantation successfully[18–20] However, there have been increased mortality rates noticed in this patient group during renal replacement therapies.[21,22]

Aim

Even though AA amyloidosis can also be related to higher mortality under renal replacement therapies,[23] most of the published experience with amyloidosis associated ESRD is about patients with AL amyloidosis and additionally, worse prognosis has been attributed to the AL amyloidosis. Hence, our objective in this study is to evaluate the clinical and laboratory characteristics of AA amyloidosis cases on hemodialysis and to help guide the management of patients with AA amyloidosis who receive maintenance hemodialysis (HD) therapy.

MATERIALS AND METHODS

Source population

We conducted a multicenter, cross-sectional, and retrospective study which was carried out in 14 selected HD centers throughout Turkey. The source population comprised 2100 patients on HD and all subjects were adults (≥18 years of age). As shown in Figure 1, 7 patients which were on hemodialysis for less than 1 year were excluded from the study. We also excluded 15 patients due to their lack of biopsy records. A total of 32 patients met the final inclusion criteria. The study was approved by the institutional review board at the Ankara University Faculty of Medicine.

Selections of cases and controls

Thirty-two patients with biopsy-proven AA amyloidosis and thirty-two control patients without AA amyloidosis undergoing HD were included between October 2018 and October 2019. We selected a comparison group of control patients whose primary renal disease was not any type of amyloidosis. Eligible control patients were individually matched to the cases based on age (±5 years) and dialysis vintage.

Measurements and data collection

Causes of AA amyloidosis, treatment (colchicine and/or anti-IL-1 treatment; canakinumab or anakinra) and the number of FMF attacks in the last year in case of FMF, systolic and diastolic blood pressures (SBP, DBP), biochemical values such as mean CRP (C-reactive protein), hemoglobin (Hgb), serum albumin, phosphorus, calcium, parathormone (PTH), ferritin, transferrin saturation, total
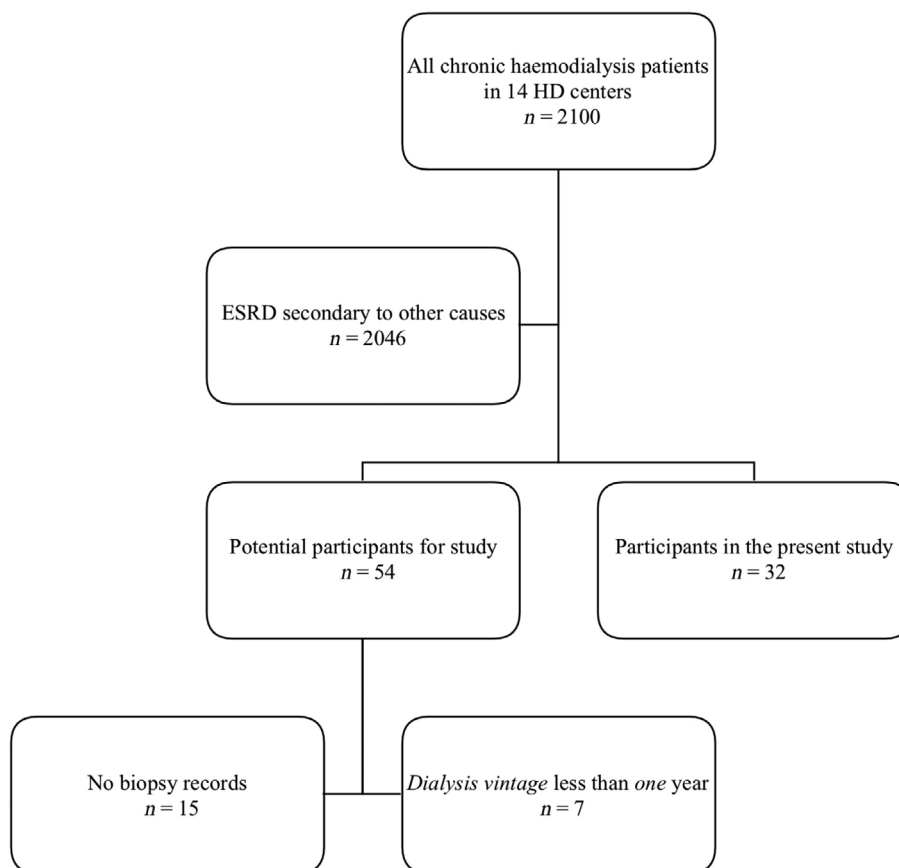

FIGURE 1 Diagram of participants enrolled in this study

cholesterol levels and erythropoietin (EPO) dose, erythropoiesis-stimulating agents (ESAs) index (ERI), interdialytic fluid intake, body mass indexes (BMI), heparin dosage, ultrafiltration (UF) volume and Kt/V data in the last year were collected by retrospective review of medical records. All BMIs were calculated by the following formula: body weight (kilograms) divided by height squared (m). A ratio of 1:200 was used to convert darbepoetin alpha to the erythropoiesis-stimulating agents (ESAs) equivalent dose (1 µg of darbepoetin alpha = 200 IU of epoetin alpha or beta). We calculated the ERI using the equation based on average weekly EPO dose per kg body weight (wt) per average Hgb, over 1 year period (ERI = [EPO/wt]/Hgb).[24] Average predialysis SBP and DBP were determined by finding the average of the predialysis SBP and DBP of the three HD sessions studied while average postdialysis SBP and DBP were determined by finding the average of the postdialysis SBP and DBP of

TABLE 1 Patients' demographic, laboratory characteristics, and clinical features in both groups

	Amyloidosis group (n = 32)	Non-amyloidosis group (n = 32)	p
Dialysis vintage (months)	104.47 ± 94.68	107.91 ± 95.22	0.885
Age (years)	54.16 ± 11.87	53.47 ± 11.56	0.815
Sex, n (%)			
Male	18 (56.3)	17 (53.1)	
Female	14 (43.8)	15 (46.9)	0.801
Vascular access, n (%)			
Fistule	31 (96.9)	25 (78.1)	
Catheter	1 (3.1)	7 (21.9)	0.053
BMI (kg/m^2)	23.10 ± 3.99	24.65 ± 3.81	0.118
Hemoglobin (g/dl)	10.94 ± 1.24	11.41 ± 0.80	0.078
CRP (mg/L)	18.78 ± 18.74	10.61 ± 10.47	**0.037***
Serum albumin (mg/dl)	3.67 ± 0.49	4.03 ± 0.22	**<0.01****
Serum calcium (mg/dl)	8.81 ± 0.57	8.90 ± 0.60	0.535
Serum phosphorus (mg/dl)	4.68 ± 0.73	5.25 ± 1.04	**0.014***
PTH (pg/ml)	364.22 ± 330.15	418.22 ± 279.60	0.483
Ferritin (ml/ng)	513.74 ± 262.21	595.90 ± 432.10	0.361
Transferrin Saturation (mg/L)	28.28 ± 6.89	29.53 ± 7.03	0.473
Total cholesterol (mg/dl)	135.66 ± 42.14	174.11 ± 39.64	**<0.01****
EPO usage, n (%)			
EPO alpha/zeta	11 (40.7)	8 (28.6)	0.343
Darbepoetin alpha	16 (59.3)	20 (71.4)	0.343
Interdialytic weight gain (kg)	2.42 ± 3.12	2.21 ± 0.87	0.711
Kt/V per week	1.94 ± 1.28	1.64 ± 0.28	0.208
Systolic BP (mmHg)	117.40 ± 22.30	121.06 ± 21.26	0.504
Diastolic BP (mmHg)	70.91 ± 10.51	72.85 ± 11.37	0.483
UF volume (ml)	2228.13 ± 864.49	2621.38 ± 824.33	0.067
Anticoagulation usage, n (%)	31 (96.9)	31 (96.9)	
Heparin	31 (100)	27 (87.1)	0.112
Enoxaparin	0	3 (9.7)	0.237
Warfarin	0	1 (3.2)	1
	Amyloidosis group (n = 30)	**Non-amyloidosis group (n = 27)**	**p**
Heparin dosage (IU/session)	2709.26 ± 866.66	3257.45 ± 1212.27	**0.05***

Note: The data are presented as the mean value ± SD or n (%) of patients. Bold values denote statistical significance at the P < 0.05 level.
*p < 0.05 is significant.
**p < 0.01 is significant.

TABLE 2 Erythropoiesis-stimulating agents (ESAs) dosing and ESAs resistance index (ERI) levels in both groups

	Amyloidosis group (n = 27)	Non-amyloidosis group (n = 28)	p
EPO alpha/zeta dosage (IU)	80.98 ± 31.93	62.01 ± 29.34	0.204
Darbepoetin dosage (IU)	0.42 ± 0.21	0.29 ± 0.16	**0.032***
ERI			
EPO alpha/zeta (IU/kg/week/g/dl)	8.07 ± 3.30	5.44 ± 2.76	0.063
Darbepoetin alpha (mcg/kg/week/g/dl)	0.39 ± 0.02	0.27 ± 0.16	**0.049***
Total ERI (IU/kg/week/g/dl)	7.88 ± 3.78	5.41 ± 3.06	**0.008****

Note: The data are presented as the mean value ± SD or n (%) of patients. Bold values denote statistical significance at the P < 0.05 level.
*$p < 0.05$ is significant.
**$p < 0.01$ is significant.

FIGURE 2 Distribution of underlying diseases causing AA amyloidosis [Color figure can be viewed at wileyonlinelibrary.com]
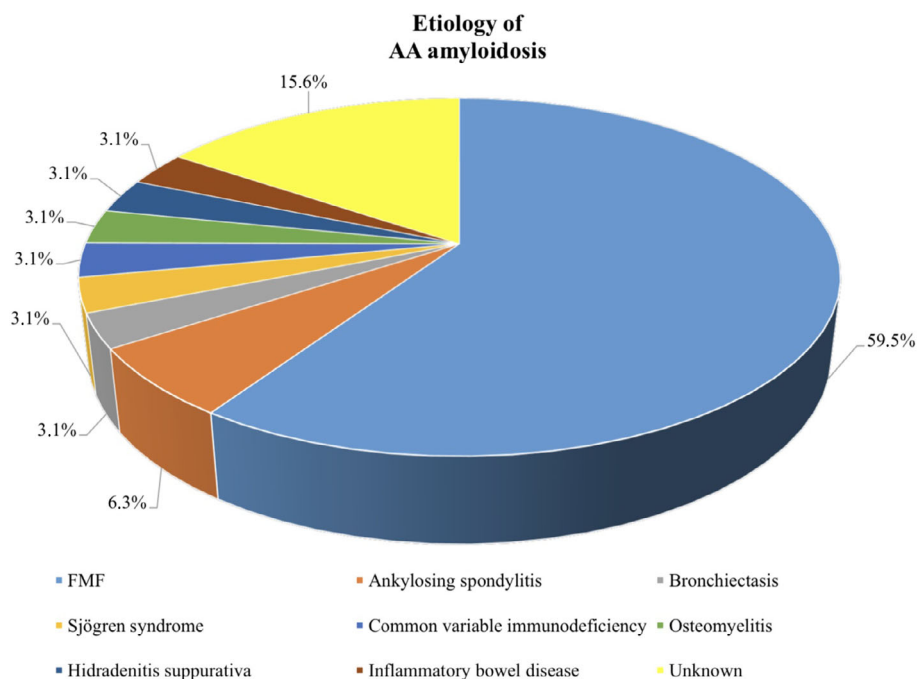
the three HD sessions studied. The Kt/V resolved from the predialysis to postdialysis urea nitrogen ratio (R), the weight loss (UF), session length in hours (t), and anthropometric or modeled volume (V).[25]

Statistical analysis

Continuous variables with normal distribution were presented as mean (standard deviation [SD]); nonparametric variables were reported as median (interquartile range [IQR]). The normality of distribution of continuous variables was tested by one-sample the Kolmogorov–Smirnov test and the Shapiro–Wilk test. Means of two continuous normally distributed variables were compared by independent samples Student's t test. The Mann–Whitney U test was used to compare medians of two groups of variables not normally distributed. Whereas the Kruskal-Wallis test was used to compare medians of three or more groups of variables. The frequencies of categorical variables were compared using x^2 or Fisher's exact test, when appropriate. Spearman's rank correlation coefficient (or Spearman's rho) was used for the nonparametric measure of the association between two continuous variables. All statistical analysis was performed using SPSS (Statistical Package for Social Science) v.18.0 software (IBM Inc., Armonk, NY). A value of $p < 0.05$ was considered significant.

RESULTS

The prevalence of AA amyloidosis among HD patients was 1.87% in HD facilities. Table 1 summarizes the baseline characteristics of all the patients in both groups. In amyloidosis and control groups, 56% and 53% were male,

mean age was 54 ± 11 and 53 ± 11 years, and mean dialysis vintage was 104 ± 94 and 107 ± 95 months, respectively. All patients received HD for 4 h in three sessions a week. In AA amyloid and control groups, total ERI was 7.88 ± 3.78 and 5.41 ± 3.06 IU/kg/week/g/dl, respectively, provided in Table 2. Figure 2 demonstrates the underlying etiology for AA amyloidosis. FMF was the most common cause of AA amyloidosis (59.5%). We have compared two subgroups (patients with AA amyloidosis secondary to FMF or patients with AA amyloidosis caused by other diseases) depending on the inflammatory marker (CRP values) and no statistical difference was found in the CRP between the *two groups* (18.85 ± 18.70 and 18.68 ± 19.56 mg/L, $p = 0.734$). All FMF patients received colchicine and the mean colchicine dose was 0.70 ± 0.30 mg/day. 26.3% of FMF patients were unresponsive to colchicine and to anti-IL-1 treatment was used in these patients (Table 3). The FMF patients were classified according to colchicine treatment response (Table 4). Despite anti-IL-1 treatment, FMF attacks were more frequent and higher CRP values were observed in potential colchicine-resistant patients. Additionally, higher CRP values (18.78 ± 18.74 and 10.61 ± 10.47 mg/L, $p = 0.037$), lower serum phosphorus (4.68 ± 0.73 vs. 5.25 ± 1.04 mg/dl, $p = 0.014$), total cholesterol (135 ± 42 vs. 174 ± 39 mg/dl, $p < 0.01$), and serum albumin (3.67 ± 0.49 mg/dl, 4.03 ± 0.22, $p < 0.01$) were observed in patients with AA amyloidosis compared to the control group (Table 1).

TABLE 3 Characteristics of FMF patients with AA amyloidosis undergoing hemodialysis during colchicine and/or anti IL-1 treatment

Colchicine usage, n (%)	AA amyloidosis (n = 32)
Yes	20 (12.5)
No	12 (37.5)
Colchicine dosage regimen, n (%)	**Colchicine users in AA amyloidosis (n = 20)**
0.5 mg/day	13 (65)
1 mg/day	6 (30)
1.5 mg/day	1 (5)
Daily colchicine dose received (mg/day)	0.70 ± 0.30
Anti-IL-1 treatment usage, n (%)	**Anti-IL-1 treatment in AA amyloidosis (n = 6)**
Anakinra	3 (50)
Canakinumab	3 (50)
Anakinra dosage (mg/week)	366.66 ± 57.73
Canakinumab dosage (mg/month)	333.33 ± 57.73

Note: The data are presented as the mean value $\pm$ SD or n (%) of patients.

TABLE 4 Characteristics of FMF patients with AA amyloidosis on hemodialysis

	Colchicine	Colchicine + anti-IL-1 treatment	*p*
FMF drug choice, n (%)	14 (73.68)	5 (26.31)	**0.035***
The frequency of FMF attacks (per year)	0.86 ± 1.83	3.20 ± 2.59	**0.032***
CRP (mg/L)	20.19 ± 20.45	15.09 ± 13.84	0.926

Note: The data are presented as the mean value $\pm$ SD or n (%) of patients. Bold values denote statistical significance at the $P < 0.05$ level.
*$p < 0.05$ is significant.

DISCUSSION

Comparison with other countries

The prevalence rates of AA amyloidosis among HD patients we found (1.87%), were almost similar to the National Nephrology, Dialysis and Transplantation Registry Report (1.76%) by The Turkish Nephrology Society at the end of 2019.[26] However, the prevalence of AA amyloidosis on HD was higher than the rates reported in developed countries.[23,27] Moreover, in Europe and the United States, AA amyloidosis in certain rheumatic diseases [mainly rheumatoid arthritis (RA), ankylosing spondylitis (AS)] are seen more often than in Turkey.[2,5] According to our study, FMF is responsible for more than half (59.5%) of patients with AA amyloidosis in Turkey. These findings suggest that the characteristics of patients with AA amyloidosis vary significantly between Turkish HD patients and HD patients in developed countries.

The UK National Amyloidosis Centre (NAC) conducted a 25-year retrospective study regarding patients with AA amyloidosis. The underlying disorders leading to AA amyloidosis were reported as follows: RA 28%, chronic infection 11%, seronegative arthritis 10%, systemic autoinflammatory diseases (SAIDs) 9%, juvenile idiopathic arthritis (JIA) 8%, inflammatory bowel disease (IBD) 5%.[27] Ensari et al. carried out immunohistochemical studies in the Turkish population on 128 biopsies from various sites of 111 patients with biopsy-proven amyloidosis and, based on the results, positivity for AA was seen in 113 of 128 biopsies (88.3%).[5] Another retrospective study, conducted by Erdogmus et al. reported that FMF is the leading cause of AA amyloidosis (62%).[15] In addition to diagnostic aid, a paper by Kendirli et al.

claimed that renal pathology in AA amyloidosis may help guide prognosis as well as establishing renal involvement of AA amyloidosis.[14]

FMF and treatment choice

FMF is an autosomal recessive autoinflammatory disease caused by the MEFV (MEditerranean FeVer) gene mutation and is characterized by brief recurrent self-limited episodic febrile attacks. FMF is more commonly seen among Turks, Arabs, Sephardic Jews, and a few other ethnic groups living in the Eastern Mediterranean basin. AA amyloidosis is the most ominous complication of late-diagnosed, untreated, or neglected FMF due to the long-lasting inflammation. Long-term prophylaxis with daily administration of colchicine effectively and safely prevents the development of AA amyloidosis. However, anti-interleukin-1 (IL-1) treatment might be a promising alternative therapeutic option for colchicine-resistant or -intolerant patients with FMF.[28,29] No consensus exists about the definition of colchicine resistance but recent studies have mainly focused on attack frequency and severity, levels of acute-phase reactants, colchicine dosage and composition, and treatment compliance.[30] In our study, potential resistance to colchicine is defined as receiving the maximum tolerated dose of colchicine or treatment with IL-1 inhibitors to prevent attacks, control symptoms, and achieve biochemical normalization of inflammatory markers due to uncontrolled active inflammation. Colchicine has a narrow therapeutic window and there is no specific antidote known for toxicity. Colchicine is not effectively removed by hemodialysis and Amanova et al. demonstrated that HD patients have elevated plasma concentrations of colchicine.[31] To improve the safety and the tolerability profile of colchicine, caution and dose reduction are required in HD patients. Regardless of whether patients received dialysis, it has been widely recognized that 5%–15% of the patients with FMF do not respond to colchicine or do not tolerate the drug.[32] According to our study, a low-dose regimen of colchicine (0.70 ± 0.30 mg/day) is ineffective in controlling inflammation and nearly one-third of all FMF patients were treated with interleukin-1 targeting drugs.

Inflammation and nutritional status

In our study, CRP negatively correlated with serum albumin, total cholesterol, and serum phosphorus. Low serum phosphate in dialysis patients, has been associated with a greater long-term risk of cardiac events with a U-shaped trend.[33] Hypoalbuminemia, hypophosphatemia can be caused by malnutrition and chronic inflammation, also known together as the malnutrition-inflammation complex syndrome (MICS). Previous studies reported that there was a strong association between higher mortality and lower serum albumin in dialysis patients.[34,35] According to Cano et al, the reported prevalence of MICS varies between 20% and 60% in dialysis patients.[36] Qureshi et al. also reported that malnutrition and inflammation predicted mortality in HD patients.[37] Our study suggests that abnormal levels of the inflammatory markers may be associated with poor prognosis in renal AA amyloidosis. Previously Palladini et al. published a study to identify the possible prognostic factors in renal AA amyloidosis. In this renal staging system for assessing overall survival; renal AA amyloid patients were divided into two groups based on age, underlying infection, and eGFR. To evaluate the renal survival; reduction of serum amyloid A (SAA) was targeted as a treatment strategy and lower SAA concentration (<10 mg/L) has also been demonstrated to be associated with better renal survival in patients on such therapy.[38] During dialysis, heparin can cause an increase in cytokine levels and several studies suggested that heparin-free dialysis might reduce the level of proinflammatory cytokines.[39,40] According to our findings in this study, despite control group patients' receiving more heparin dose than the amyloidosis group, inflammatory markers were observed significantly elevated in AA amyloidosis patients. Starting from this point of view, if both groups had not received a different dosage of heparin, this difference between groups would be more prominent. We also noticed that there is no difference between the underlying causes of AA amyloidosis (AA amyloid caused by FMF versus patients with AA amyloidosis caused by other diseases) in terms of inflammatory markers.

Hyporesponsiveness to erythropoiesis-stimulating agent therapy

Erythropoiesis-stimulatory agents (ESAs) resistant anemia in HD patients is a significant and frequent problem. Zhang et al. demonstrated that inadequate response to ESAs among HD patients was associated with increased mortality.[41] Recently, usage of the ESAs index (ERI) has been proposed to normalize the amount of ESAs required depending on the severity of anemia and ERI can be considered a prognostic factor in HD patients.[42] We found that the AA amyloidosis group receiving darbepoetin (DPO) statistically possessed significantly higher ERI ($p = 0.049$) compared to the control group. Whereas there was no statistically significant difference in the AA amyloidosis group receiving erythropoietin (EPO) alpha/

zeta ($p = 0.063$). The p-value was close; however, the EPO group did not reach statistical significance. It is difficult to determine whether there is a significant statistical difference between groups due to most participants receiving DPO in both groups. Thus, we developed and calculated a total ERI to make a comparison of groups ERI among different ESAs. And we have found that AA amyloidosis patients had significantly higher total ERI ($p = 0.008$).

CONCLUSION

In summary, we have confirmed the prevalence rates and leading causes of AA amyloidosis and the potential predictors of mortality in the Turkish population with AA amyloidosis in HD facilities. Our results suggest that several inflammatory and nutritional markers including blood C-reactive protein, serum albumin, and serum phosphorus levels may be identified as prognostic factors in HD patients with AA amyloidosis. In addition to this, ERI calculation may have potential clinical utility as a prognostic tool that could help on the risk evaluation of AA amyloidosis patients undergoing HD. We, therefore, speculate that the vicious cycle of malnutrition, inflammation, and atherosclerosis (MIA syndrome) may worsen the patient outcome for patients with AA amyloidosis on HD. Anti-cytokine therapies may contribute not only to the effective treatment of AA amyloidosis but also to improve prognosis in dialysis patients. Despite anti-IL-1 inhibitors, the potential colchicine-resistant patients have higher levels of inflammatory markers. It can be associated with the degree of sustained inflammation. In this context, severe inflammation in AA amyloidosis patients may accelerate progression to end-stage renal disease. Further studies including a long-term prospective study will be required to assess the prognostic markers and mortality of patients with AA amyloidosis receiving HD.

CONFLICT OF INTEREST
The authors declare that there is no conflict of interest.

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