ORIGINAL ARTICLE

Impact of Hemodialysis on Serum Fluorescent Advanced Glycation End-products in End-stage Renal Disease Patients

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Abstract

Introduction: Serum fluorescent advanced glycation end-product (AGE) levels are independent predictors of cardiovascular and all-cause mortality risks in end-stage renal disease (ESRD). The present study aimed to estimate the impact of hemodialysis (HD), a common treatment modality, on serum fluorescent AGEs. **Materials and Methods:** 68 ESRD HD patients were included in the cross-sectional study, which had 37 non-diabetics and 31 diabetics. Serum fluorescence of total, Pentosidine, and low molecular weight (LMW) AGEs were measured pre- and post-HD. **Results:** Paired *t*-test comparisons showed significant decreases in post-HD fluorescence of total AGEs (by 1394.3 arbitrary units [AU]), Pentosidine (by 1028.5 AU), and LMW AGEs (by 328.2 AU); $P < 0.001$, compared to their pre-HD levels in the ESRD patients. Independent t-test comparisons showed significantly higher pre-HD total AGEs in non-diabetic than in diabetic ESRD patients (4639.9 AU vs. 3857.16 AU; $P = 0.004$). Pre-HD Pentosidine level was also significantly higher in non-diabetic than in diabetic ESRD patients (3072.97 AU vs. 2513.01 AU; $P = 0.009$) who took antidiabetic medications. **Discussion:** These findings demonstrate the positive impact of the given standard HD therapy in decreasing AGE levels and potentially, the AGE-associated risks. Lower pre-dialysis AGE levels observed in diabetic patients receiving antidiabetic therapy suggest a potential adjunctive protective effect that warrants further investigation. **Conclusion:** HD significantly reduces AGE levels in ESRD patients, underscoring its beneficial role in mitigating AGE-associated cardiovascular risk. The higher AGE levels in non-diabetic ESRD patients emphasize the need for subgroup-specific therapeutic strategies.

Key words: Advanced-glycation-end-products, end-stage renal disease, hemodialysis, low-molecular-weight advanced glycation end products, pentosidine, serum fluorescence

INTRODUCTION

Chronic kidney disease (CKD) is the 12th leading cause of death worldwide and a significant public health burden.[1] Decline in renal function is associated with an increase in morbidity and mortality in CKD subjects, which is primarily attributable to cardiovascular disease (CVD).[2] The prognosis deteriorates in individuals with CKD stage 5 or end-stage renal disease (ESRD). Hemodialysis (HD) is a common renal replacement therapeutic modality for ESRD. HD-dependent uremic individuals have a roughly 15-fold higher risk of mortality due to CVD than the general population, even after controlling for conventional risk factors.[3] Accumulation of advanced glycation end-products (AGEs) has been proposed to lead to

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endothelial dysfunction and accelerated cardiovascular risks in chronic renal disease and dialysis, irrespective of the presence of diabetes mellitus.[4-7] Apart from diabetes mellitus, excessive oxidative stress, chronic inflammation, diet, and reduced renal clearance, which occur in CKD, can cause accumulation of AGEs, such as Pentosidine, N-carboxymethyllysine, and N-carboxyethyllysine, many of which are fluorescent and produced through non-enzymatic glycation and glycoxidation of proteins, nucleic acids, and lipid biomolecules.[8-10]

Pentosidine, a well-characterized AGE, derived from ribose sugar, forms fluorescent cross-links in collagen, the primary structural protein of connective tissues in the human body. Serum pentosidine was found to be positively associated with arterial stiffness, thickness, and CVD in type 2 diabetes mellitus.[11] Low molecular weight (LMW) AGEs, also referred to as AGE peptides, or LMW-fluorophores, are AGE-modified proteins that have undergone partial breakdown. LMW AGEs have a high potential for toxicity, and their circulating levels are indicators of tissue AGEs.[12] LMW AGE fluorescence has been reported to predict mortality in asymptomatic patients receiving chronic HD.[13]

Fluorescent AGEs are also independently associated with all-cause mortality in ESRD patients without any difference observed between diabetic and non-diabetic patients.[14-17] HD *per se* can induce oxidative stress due to the activation of immune cells, release of pro-inflammatory cytokines, and exposure to bioincompatible dialysis membranes and tubing.[18-20] Assessment of the impact of HD on serum AGE levels is pivotal for the proper management of ESRD patients due to the associated cardiovascular and all-cause mortality risks, which are among the four core HD outcome domains identified.[21] However, there are limited reports in the literature on the same, particularly in the Indian population. The present study objective was to estimate and compare the pre-post HD levels of total fluorescent AGEs, Pentosidine, and LMW AGEs in ESRD patients with and without diabetes mellitus.

MATERIALS AND METHODS

Study design and participants

The study design was cross-sectional and included 68 ESRD male and female patients with and without diabetes mellitus, aged 40–60 years, who attended the nephrology department for routine HD therapy, at a tertiary care hospital, in the Dakshina Kannada district of Karnataka State, India. Chronic alcoholics, pre-diabetic, decompensated chronic liver disease subjects, and those under treatment with immunosuppressive drugs, with active and advanced cancer on cancer therapy, who had undergone recent hospitalization or surgery, or seriously ill, were excluded. The study was conducted after obtaining approval from the Institutional Ethics Committee in accordance with the Declaration of Helsinki (2013) guidelines; vide YEC-1/635/2023. Every participant in the study gave their informed consent.

Sample collection

4 mL of blood was collected from each study participant 15 min before the start of HD therapy as pre-HD samples. 4 mL of post-HD blood samples were collected from each subject 15 min post-HD cycle, typically of 4 h duration. After allowing the blood samples to coagulate, they were centrifuged for 15 min at 3000 rpm. The serum supernatants were collected and temporarily stored in the fridge at 4°C till assayed further for AGEs.

Clinical laboratory data

Clinical laboratory values of blood glucose, hemoglobin (Hb), calcium, phosphorous, creatinine, and urea were obtained from the routine clinical laboratory reports of the study participants.

Measurement of fluorescent AGEs

Total serum fluorescent AGEs were estimated by standard measurements of their fluorescence in a Hitachi spectrofluorimeter with excitation at 370 nm wavelength and at 440 nm emission wavelength. Pentosidine fluorescence was measured with excitation at 335 nm wavelength and at 385 nm emission wavelength. For LMW AGEs, 100 µL of undiluted sera were pre-treated by deproteinizing with 100 µL of 5% trichloroacetic acid, then mixing by vortexing, incubating at room temperature for 10 min, and centrifuging at 8000 rpm (5000 × g) for 20 min. The supernatants were used for fluorescence measurements at excitation at 370 nm and emission at 440 nm wavelengths, respectively. Serum total AGE, Pentosidine, and LMW AGE fluorescence values were expressed in arbitrary units as per the standard procedures.[22]

Statistical analysis of data

Analysis and plotting of data were performed statistically using the Statistical Package for the Social Sciences version 27 and GraphPad Prism version 10.0. Descriptive measures were used to estimate the study factors. The categorical variable was compared using the Chi-square test. The comparison of pre-post HD mean values for total AGEs, Pentosidine, and LMW AGEs was conducted using a paired *t*-test, as these measurements were found to follow a normal distribution. The comparison of means for total AGEs, Pentosidine, and LMW measurements between non-diabetic and diabetic groups utilized the independent *t*-test due to adherence to a normal distribution.

Pre-HD as well as post-HD mean values of total, Pentosidine AGEs, and LMW AGEs were separately compared between diabetic and non-diabetic ESRD patients by independent *t*-tests. Mean differences between pre- and post-HD AGE values were compared between non-diabetic and diabetic ESRD patients by an independent *t*-test. The impact of HD

therapy on serum fluorescent total AGEs, Pentosidine, and LMW AGEs was assessed based on the differences in their respective pre-post HD levels.

RESULTS

Baseline features of participants in the study

Among the studied 68 ESRD HD patients, there were 37 non-diabetics and 31 diabetics, with a higher proportion of males in both non-diabetic and diabetic ESRD subgroups. Demographic, biochemical and clinical data of all the ESRD HD patients included in the study and the subgroups, categorized according to their diabetic status [Table 1].

Among all the baseline characteristics of the studied ESRD patients, only plasma glucose levels showed statistically significant difference between non-diabetic and diabetic subgroups of ESRD patients with $P < 0.0001$****. Random plasma glucose levels of diabetic ESRD were significantly higher than that of non-diabetic ESRD patients. The mean Hb

Table 1: Baseline characteristics of study participants

Variables	ESRD HD study group	Subgroups of ESRD HD patients		*P*-value
		Non-diabetic	Diabetic	
Number of participants	68	37	31	-
Age (years)[a]	52±6	51±6	53±6	0.2799
Male/female, *n* (%)[b]	51/17 (75/25)	25/12 (68/32)	26/5 (84/16)	0.1220
Cycles of dialysis/week (%)				-
Twice	24	32	13	
Thrice	76	68	87	
Average diabetes duration (years)	-	-	15.32	-
Hypoglycemic agents used, *n* (%)	31 (46)	0	31 (100)	-
Subcutaneous-insulin			19 (61)	
Oral-Glimepiride/reclide			7 (23)	
Teneligliptin			5 (16)	
Random plasma glucose (mg/dL)[a] 80–130	145.28±61.44	107.38±24.07	190.52±62.03	**<0.0001****
Hemoglobin (g/dL)[a] Males 13–17, females 12–15	9.29±1.37	9.43±1.45	9.13±1.28	0.3760
Serum creatinine (mg/dL)[a] Males 0.62–1.1, females 0.52–1.04	9.33±3.48	9.85±4.19	8.71±2.29	0.1773
Blood urea (mg/dL)[a] Males 19–43, females 15–36	96.15±45.17	101.73±51.98	89.48±35.09	0.2686
Serum phosphorous (mg/dL)[a] 2.5–4.5	6.31±1.91	6.31±1.82	6.32±2.04	0.9813
Serum calcium (mg/dL)[a] 8.4–10.2	7.73±1.14	7.54±1.37	7.97±0.76	0.1288
Hypertension, *n* (%)	59 (87)	28 (76)	31 (100)	-
Hypoglycemic agents used, *n* (%)	31 (46)	0	31 (100)	-
Subcutaneous-insulin			19 (61)	
Oral-Glimepiride/reclide			7 (23)	
Teneligliptin			5 (16)	
Antihypertensives used, *n* (%)				
Blockers of calcium channel	18 (30)	-	-	-
Inhibitors of angiotensin-converting enzyme	17 (29)			
β-blockers	14 (24)			
Blockers of angiotensin receptor	10 (17)			

[a]Data represent mean±SD. $p<0.05$ is considered as statistically significant. $p < 0.0001$ is bolded and denoted as ****. Non diabetic ESRD versus diabetic ESRD subgroup comparisons of variables are analyzed by independent *t* test and bcategorical variable is analyzed by the Chi square test. Biological reference intervals of biochemical variables are given below their respective names. ESRD: End stage renal disease, HD: Hemodialysis, SD: Standard deviation

values of ESRD patients were low, indicating the presence of anemia. Mean values of renal function parameters, serum creatinine, urea and phosphorus were high, while calcium levels were low [Table 1].

Pre-HD and post-HD serum fluorescent AGEs levels of ESRD patients

The pre- and post-HD levels of serum fluorescent total, Pentosidine, and LMW AGEs of all 68 ESRD patients, irrespective of their diabetic status, were compared [Figure 1].

Highest pre-HD mean fluorescence values were obtained for total AGEs, intermediate for Pentosidine, and the lowest for LMW AGEs. Post-HD fluorescence values also showed the same pattern, with the highest mean fluorescence values for total AGEs, intermediate for Pentosidine, and the least with LMW AGEs. The post-HD serum fluorescence levels of total, Pentosidine, and LMW AGEs were all significantly decreased compared to their respective pre-HD levels with $P < 0.0001$**** in the studied ESRD patients [Figure 1].

The mean differences between pre- and post-HD levels of serum fluorescent total AGEs, Pentosidine, and LMW AGEs of all the studied ESRD patients, irrespective of their diabetic status, are shown in Figure 2. The mean differences are positive values for all the studied AGEs as their respective pre-HD levels were statistically significantly higher with $P < 0.0001$**** than their post-HD levels [Figure 1]. Highest mean difference was obtained for total AGEs, intermediate for Pentosidine, and the least difference was obtained for LMW AGEs [Figure 2].

Pre-HD and post-HD serum fluorescent AGEs levels of non-diabetic ESRD and diabetic subgroups of ESRD patients

Next, the pre-HD fluorescence values of total, Pentosidine, and LMW AGEs were compared between non-diabetic and diabetic ESRD patients [Figure 3]. Similarly, the post-HD fluorescence values of total, Pentosidine, and LMW AGEs were compared between non-diabetic and diabetic ESRD patients [Figure 3]. The pre-HD values of non-diabetic ESRD patients were found to be significantly higher compared to diabetic ESRD patients for total AGEs, with $P = 0.007$** and also for Pentosidine, with $P = 0.0186$*. For LMW AGEs, although the pre-HD fluorescence levels in non-diabetic ESRD were also found to be higher compared to diabetic ESRD patients, they were not significant statistically, with $P = 0.3671$. Like with pre-HD levels, the post-HD mean fluorescence values were also found to be higher in non-diabetic individuals with ESRD than in diabetic patients with ESRD but, the results were not significant statistically for total AGEs ($P = 0.1176$) and Pentosidine, with $P = 0.4027$. Post-HD mean fluorescence value of LMW AGEs, unlike their pre-HD mean fluorescence value, was lower in ESRD

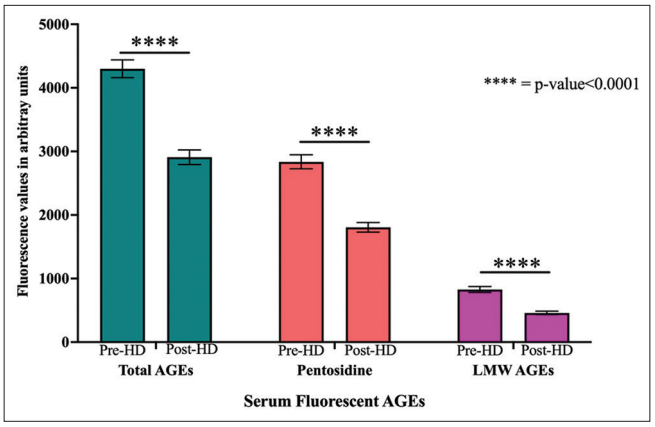

Figure 1: Comparison of pre-hemodialysis and post-hemodialysis levels of serum fluorescent advanced glycation end-product in end-stage renal disease patients. Data represent mean ± standard error of the mean values ($n = 68$). $p < 0.05$ is considered as statistically significant. $p < 0.0001$ is bolded and denoted as ****. Paired *t*-test was used for the comparisons.

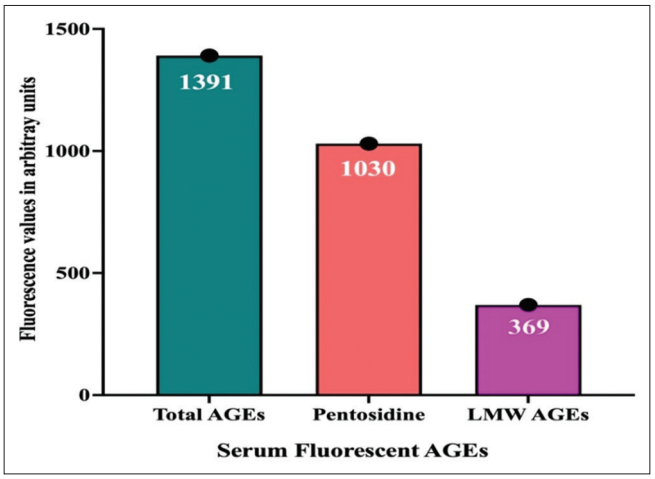

Figure 2: Post-hemodialysis decreases in serum fluorescent advanced glycation end-product (AGE) levels of end-stage renal disease (ESRD) patients. Pre-post hemodialysis mean differences in fluorescence values are given for total AGEs, Pentosidine and low molecular weight AGEs in ESRD patients ($n = 68$)

patients without diabetes, than in those with diabetes, but was not statistically significant, with $P = 0.0946$ [Figure 3].

In non-diabetic ESRD patients, post-HD, fluorescence levels decreased by 33.8%, 39.3% and 52%, respectively, for total AGEs, Pentosidine, and LMW AGEs. Whereas in diabetic ESRD patients the decreases were by 30.3%, 32% and 34.8% for total AGEs, Pentosidine, and LMW AGEs, respectively.

Figure 4 gives the mean differences in fluorescence values between pre- and post-HD levels of serum total AGEs, Pentosidine, and LMW AGEs of non-diabetic ESRD and diabetic ESRD patients. The pre-post-HD mean differences of fluorescence values were found to be significantly higher

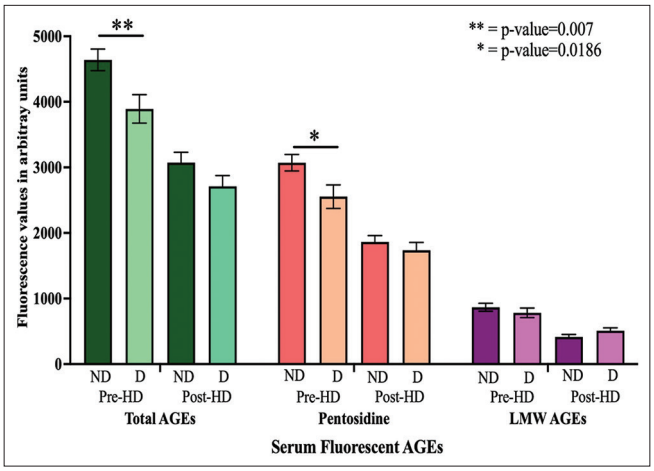

Figure 3: Comparisons of pre-hemodialysis and post-hemodialysis (Pre-HD and Post-HD) levels of serum fluorescent advanced glycation end-product (AGEs) between non-diabetic end-stage renal disease (ESRD) and diabetic ESRD patients. Pre-HD and Post-HD serum fluorescence levels of total AGEs, Pentosidine and low molecular weight AGEs of non-diabetic (ND) ESRD (n = 37) and diabetic (D) ESRD patients (n = 31) are shown. Data represent mean ± standard error of the mean values. p < 0.05 is considered to be statistically significant. Significant changes are bolded, denoted as ** for p = 0.007 and * for p = 0.0186. Mean value comparisons between ND ESRD and D ESRD subgroups were done using Independent *t*-tests for total AGEs, Pentosidine and low molecular weight AGE measurements.

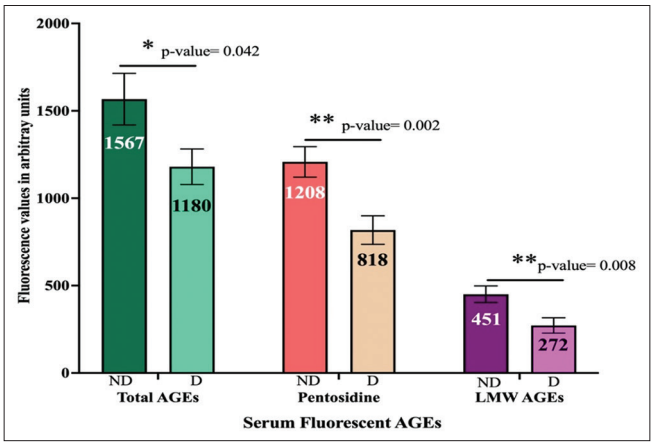

Figure 4: Comparisons of post-hemodialysis decreases in serum fluorescent advanced glycation end-product (AGE) levels between non-diabetic end-stage renal disease (ESRD) and diabetic ESRD patients. Post-hemodialysis decreases in serum fluorescent AGE levels of non-diabetic (ND) ESRD (n = 37) and diabetic (D) ESRD patients (n = 31) are shown. Data represent mean differences ± standard errors of mean differences in pre-post hemodialysis fluorescence values of total AGEs, Pentosidine, and low molecular weight AGEs for ND ESRD and D ESRD patients. p < 0.05 is considered to be statistically significant. Significant changes are bolded, denoted as *for p = 0.042, **for p = 0.002 and 0.008. Mean difference comparisons between the two ESRD subgroups were done using independent *t*-tests.

in ESRD patients without diabetes compared to those with diabetes for total AGEs with P = 0.042*, Pentosidine with P = 0.002**, and LMW AGEs with P = 0.008**. The mean differences are positive values for all the studied AGEs in ESRD patients as their respective pre-HD levels were higher than their post-HD levels, irrespective of their diabetes status [Figure 4].

DISCUSSION

ESRD and HD, both, are associated with heightened cardiovascular and all-cause mortality risks.[2,3] Alongside conventional risk factors, excessive oxidative stress and chronic inflammation are contributors to increased mortality associated with ESRD.[23,24] Reactive oxygen intermediates (ROIs) generated during AGE modification could play a significant role in oxidative stress. AGEs, formed by non-enzymatic reactions between sugars and proteins, are known to undergo modifications that lead to the generation of ROIs.[25-27]

One of the main findings of this study is that HD therapy resulted in significant decreases in total serum fluorescent AGEs, Pentosidine, as well as the LMW AGE levels of the study participants with ESRD. These findings are encouraging as they demonstrate the positive impact of the given standard HD therapy, especially with LMW AGEs formed through the incomplete degradation of AGE-modified proteins, which may be more toxic than the larger AGEs due to their possible interactions with more distant tissue receptors through the circulation.[12] As AGE accumulation is an independent indicator of mortality from all causes in CKD, reduction in their levels due to HD as demonstrated in the ESRD patients of this study, can result in a decrease in their all-cause mortality risks. According to the present knowledge, there are no other previous reports in literature which have estimated and compared the pre-post HD changes in serum fluorescent total AGEs, Pentosidine, as well as LMW AGEs in the same ESRD patients.

ESRD HD patients with diabetes constituted 46% of the total ESRD patients on HD in this study. Interestingly, the present study results demonstrated significantly higher pre-HD total serum fluorescent AGEs and Pentosidine levels in ESRD HD patients without diabetes than in those with diabetes. The possible cause for this is effect is the intake of prescription anti-diabetic medications by all the 31 diabetic ESRD study participants for their diabetic control. This finding emphasizes the potential pleiotropic benefits of antidiabetic therapy in modulating AGE levels, beyond the expected glycemic control. Several commonly used hypoglycemic medications, including metformin, pioglitazone, reclide (sulfonylurea class), dipeptidyl peptidase-4 inhibitors (gliptin class) and certain phytotherapeutic agents have been reported to decrease the AGE levels.[28-30] The results of the present

study vary from that of previous studies in which advanced CKD patients aged more than 65 years, not yet on dialysis but on conservative therapy with relatively stable estimated glomerular filtration rate, did not show any significant differences in total fluorescent AGEs between diabetic and non-diabetic persons.[15,17] However, information about the medication intake by the diabetic CKD patients is lacking in those studies.

Like with total serum fluorescent AGEs and Pentosidine levels, the pre-HD serum fluorescence of LMW AGEs were also found to be higher in ESRD HD patients without diabetes than in those with diabetes in this study which could be due to the effect of antidiabetic medications in diabetic ESRD patients. However, the changes were not statistically significant. This emphasizes the need for improved therapeutic strategies to lower the LMW AGE levels in both diabetic and non-diabetic ESRD patients. LMW AGEs were reported to be significantly higher in diabetic than non-diabetic normal subjects in a previous study, which did not include ESRD or HD patients, although some degree of renal dysfunction was present in the diabetic patients.[31] Higher circulating LMW AGEs in those diabetic patients were shown to be primarily determined by the renal dysfunction indicators albumin/creatinine ratio in urine and creatinine in serum. Details of antidiabetic medication or its possible effect were not given in the previous report.

Comparison of the post-HD total, Pentosidine, and LMW AGEs levels between non-diabetic and diabetic ESRD HD patients in the present study did not reveal any statistically significant differences. Post-HD mean levels of total AGEs and Pentosidine were higher in non-diabetic than in diabetic ESRD HD patients, possibly due to higher pre-HD levels found in them. LMW AGEs showed a different pattern, with lower post-HD mean levels in ESRD patients without diabetes than in those with diabetes, but being statistically non-significant. The precise explanations of this unfavorable impact of HD on LMW AGEs in diabetic ESRD patients need to be further investigated.

Comparison of the mean difference of pre-post HD fluorescence values of AGEs between non-diabetic and diabetic ESRD patients showed statistically significant changes for total AGEs, Pentosidine and LMW AGEs. The percentage decrease in all types of AGEs after HD was more in non-diabetic than in diabetic ESRD patients, which can be attributed to their higher pre-HD values. The significant reduction in AGE levels achieved through HD as demonstrated in the present study, may offer clinical benefits, potentially reducing CVD burden and mortality risks and improving overall health outcomes for ESRD individuals undergoing this treatment.[21] However, it is possible for the AGE levels to rise between HD cycles. This underscores the importance of improved screening, monitoring and management of serum fluorescent AGE levels in ESRD patients. The findings of this study provide key implications for the management of individuals with ESRD undergoing HD, particularly in the context of the potential beneficial effect of antidiabetic medications on AGE levels. Although AGEs and the AGE-associated CVD risks in ESRD patients can decrease after HD, other non-traditional factors, such as electrolyte disturbances, cardiovascular calcifications, intradialytic volume overload, anemia and ventricular hypertrophy which occur in ESRD HD patients may contribute to their high CVD and mortality risks erythropoietin deficiency due to renal failure can result in anemia, which was found to be present in diabetic as well as non-diabetic ESRD patients in the present study.[32] The observed differences in fluorescent AGE levels between ESRD patients with and without diabetes underscore the importance of individualized treatment approaches tailored to the specific needs of the patient subgroup. Future research needs to focus on elucidating the mechanisms and exploring targeted interventions for reducing the pre-HD AGE levels in non-diabetic ESRD patients and improving their clinical outcomes.

CONCLUSION

The study findings demonstrate that HD significantly reduces serum fluorescent AGE levels, including total AGEs, Pentosidine, and LMW AGEs, in ESRD patients, with and without diabetes, thereby potentially lowering their AGE-associated cardiovascular and all-cause mortality risks. Higher pre-HD AGE levels found in ESRD patients without diabetes compared to those with diabetes, suggests a possible modulatory effect of antidiabetic medications which underscores the need for subgroup-specific management approaches. Regular monitoring of serum fluorescent AGEs may serve as a valuable tool for optimizing dialysis regimens, evaluating treatment efficacy, and guiding personalized therapeutic interventions aimed at improving clinical effects in the ESRD population.

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AUTHORS' CONTRIBUTIONS

N.L.R: Study conceptualization, reviewing of literature, methodology, supervision, intellectual input, interpretation, writing-reviewing, and editing. A.N: Reviewing of literature, conduction of experiments, compilation of data, analyzing and writing. B. H. S.P: Clinical inputs and reviewing. C.D: Reviewing, editing, and submission of manuscript. R.D: Reviewing, data analysis, and plotting graphs.

ETHICAL APPROVAL

This study received approval from the Yenepoya Medical College Institutional Ethics Committee (YEC-1/635/2023) and was conducted in accordance with the Declaration of Helsinki (2013) guidelines.

INFORMED CONSENT

All participants provided written informed consent for the study and publication of the data.

REFERENCES

1. Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, *et al*. Global, regional, and national burden of chronic kidney disease, 1990-2017: A systematic analysis for the global burden of disease study 2017. Lancet 2020;395:709-33.
2. Matsushita K, Coresh J, Sang Y, Chalmers J, Fox C, Guallar E, *et al*. Estimated glomerular filtration rate and albuminuria for prediction of cardiovascular outcomes: A collaborative meta-analysis of individual participant data. Lancet Diabetes Endocrinol 2015;3:514-25.
3. Ortiz A, Covic A, Fliser D, Fouque D, Goldsmith D, Kanbay M, *et al*. Epidemiology, contributors to, and clinical trials of mortality risk in chronic kidney failure. Lancet 2014;383:1831-43.
4. Martens RJ, Broers NJ, Canaud B, Christiaans MH, Cornelis T, Gauly A, *et al*. Relations of advanced glycation endproducts and dicarbonyls with endothelial dysfunction and low-grade inflammation in individuals with end-stage renal disease in the transition to renal replacement therapy: A cross-sectional observational study. PLoS One 2019;14:e0221058.
5. Saum K, Campos B, Celdran-Bonafonte D, Nayak L, Sangwung P, Thakar C, *et al*. Uremic advanced glycation end products and protein-bound solutes induce endothelial dysfunction through suppression of Krüppel-like factor 2. J Am Heart Assoc 2018;7:e007566.
6. Calviño J, Cigarran S, Gonzalez-Tabares L, Menendez N, Latorre J, Cillero S, *et al*. Advanced glycation end products (AGEs) estimated by skin autofluorescence are related with cardiovascular risk in renal transplant. PLoS One 2018;13:e0201118.
7. Linden E, Cai W, He JC, Xue C, Li Z, Winston J, *et al*. Endothelial dysfunction in patients with chronic kidney disease results from advanced glycation end products (AGE)-mediated inhibition of endothelial nitric oxide synthase through RAGE activation. Clin J Am Soc Nephrol 2008;3:691-8.
8. Ahmed N. Advanced glycation endproducts--role in pathology of diabetic complications. Diabetes Res Clin Pract 2005;67:3-21.
9. Goldin A, Beckman JA, Schmidt AM, Creager MA. Advanced glycation end products: Sparking the development of diabetic vascular injury. Circulation 2006;114:597-605.
10. Leurs P, Lindholm B. The AGE-RAGE pathway and its relation to cardiovascular disease in patients with chronic kidney disease. Arch Med Res 2013;44:601-10.
11. Yoshida N, Okumura K, Aso Y. High serum pentosidine concentrations are associated with increased arterial stiffness and thickness in patients with type 2 diabetes. Metabolism 2005;54:345-50.
12. Deuther-Conrad W, Franke S, Sommer M, Henle T, Stein G. Differences in the modulating potential of advanced glycation end product (AGE) peptides versus AGE proteins. Kidney Int Suppl 2001;78:S63-6.
13. Roberts MA, Thomas MC, Fernando D, Macmillan N, Power DA, Ierino FL. Low molecular weight advanced glycation end products predict mortality in asymptomatic patients receiving chronic haemodialysis. Nephrol Dial Transplant 2006;21:1611-7.
14. Machowska A, Sun J, Qureshi AR, Isoyama N, Leurs P, Anderstam B, *et al*. Plasma pentosidine and its association with mortality in patients with chronic kidney disease. PLoS One 2016;11:e0163826.
15. Dozio E, Vettoretti S, Caldiroli L, Nerini-Molteni S, Tacchini L, Ambrogi F, *et al*. Advanced glycation end products (AGE) and soluble forms of AGE receptor: Emerging role as mortality risk factors in CKD. Biomedicines 2020;8:638.
16. Koska J, Gerstein HC, Beisswenger PJ, Reaven PD. Advanced glycation end products predict loss of renal function and high-risk chronic kidney disease in type 2 diabetes. Diabetes Care 2022;45:684-91.
17. Molinari P, Caldiroli L, Dozio E, Rigolini R, Giubbilini P, CorsiRomanelli MM, *et al*. Association between advanced glycation end-products and sarcopenia in patients with chronic kidney disease. Biomedicines 2022;10:1489.
18. Descamps-Latscha B, Drüeke T, Witko-Sarsat V. Dialysis-induced oxidative stress: Biological aspects, clinical consequences, and therapy. Semin Dial 2001;14:193-9.
19. Descamps-Latscha B, Goldfarb B, Nguyen AT, Landais P, London G, Haeffner-Cavaillon N, *et al*. Establishing the relationship between complement activation and stimulation of phagocyte oxidative metabolism in hemodialyzed patients: A randomized prospective study. Nephron 1991;59:279-85.
20. Nguyen AT, Lethias C, Zingraff J, Herbelin A, Naret C, Descamps-Latscha B. Hemodialysis membrane-induced activation of phagocyte oxidative metabolism detected *in vivo* and *in vitro* within microamounts of whole blood. Kidney Int 1985;28:158-67.
21. Bello AK, Okpechi IG, Osman MA, Cho Y, Htay H, Jha V, *et al*. Epidemiology of haemodialysis outcomes. Nat Rev Nephrol 2022;18:378-95.
22. Indyk D, Bronowicka-Szydełko A, Gamian A, Kuzan A. Advanced glycation end products and their receptors

in serum of patients with type 2 diabetes. Sci Rep 2021;11:13264.
23. Liakopoulos V, Roumeliotis S, Gorny X, Dounousi E, Mertens PR. Oxidative stress in hemodialysis patients: A review of the literature. Oxid Med Cell Longev 2017;2017:3081856.
24. Lee HB, Yu MR, Yang Y, Jiang Z, Ha H. Reactive oxygen species-regulated signaling pathways in diabetic nephropathy. J Am Soc Nephrol 2003;14:S241-5.
25. Sakurai T, Tsuchiya S. Superoxide production from nonenzymatically glycated protein. FEBS Lett 1988;236:406-10.
26. Araki N, Higashi T, Mori T, Shibayama R, Kawabe Y, Kodama T, *et al*. Macrophage scavenger receptor mediates the endocytic uptake and degradation of advanced glycation end products of the Maillard reaction. Eur J Biochem 1995;230:408-15.
27. Chen MF, Chang CL, Liou SY. Increase in resting levels of superoxide anion in the whole blood of uremic patients on chronic hemodialysis. Blood Purif 1998;16:290-300.
28. Mirmiranpour H, Mousavizadeh M, Noshad S, Ghavami M, Ebadi M, Ghasemiesfe M, *et al*. Comparative effects of pioglitazone and metformin on oxidative stress markers in newly diagnosed type 2 diabetes patients: A randomized clinical trial. J Diabetes Complications 2013;27:501-7.
29. Sakata K, Hayakawa M, Yano Y, Tamaki N, Yokota N, Eto T, *et al*. Efficacy of alogliptin, a dipeptidyl peptidase-4 inhibitor, on glucose parameters, the activity of the advanced glycation end product (AGE) - receptor for AGE (RAGE) axis and albuminuria in Japanese type 2 diabetes. Diabetes Metab Res Rev 2013;29:624-30.
30. Jud P, Sourij H. Therapeutic options to reduce advanced glycation end products in patients with diabetes mellitus: A review. Diabetes Res Clin Pract 2019;148:54-63.
31. Sharp PS, Rainbow S, Mukherjee S. Serum levels of low molecular weight advanced glycation end products in diabetic subjects. Diabet Med 2003;20:575-9.
32. Cozzolino M, Mangano M, Stucchi A, Ciceri P, Conte F, Galassi A. Cardiovascular disease in dialysis patients. Nephrol Dial Transplant 2018;33:iii28-34.

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