Age and Ageing 2009; **38:** 283–289
doi: 10.1093/ageing/afp011
Published electronically 28 February 2009

Elevated serum advanced glycation end products and their circulating receptors are associated with anaemia in older community-dwelling women

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Abstract

Objective: to determine whether serum carboxymethyl-lysine, a dominant advanced glycation end product (AGE), and circulating total receptor for AGEs (sRAGE) and endogenous secretory receptor for AGEs (esRAGE) are associated with anaemia.
Design: cross-sectional analysis.
Setting: moderately severely disabled women, ≥65 years, living in the community in Baltimore, MD (the Women's Health and Aging Study I).
Participants: 519 women with and without anaemia.
Main outcome measure: haemoglobin and anaemia (haemoglobin <12 g/dL).
Results: of 519 women, 128 (24.7%) had anaemia. All odds ratios (OR) were expressed per one standard deviation. Serum CML was associated with anaemia [OR 1.47, 95% confidence interval (CI) 1.11–1.95, $P = 0.008$] in a multivariate logistic regression model adjusting for age, race, smoking, education and chronic diseases. Serum sRAGE (ng/mL) and esRAGE (ng/mL) were associated with anaemia (OR 1.52, 95% CI 1.21–1.92, $P = 0.0004$; OR 1.49, 95% CI 1.18–1.87, $P = 0.0006$, respectively) in separate multivariate logistic regression models, adjusting for the same covariates mentioned above. Serum CML ($P = 0.004$), sRAGE ($P < 0.0001$) and esRAGE ($P < 0.0001$) were inversely and independently associated with haemoglobin concentrations.
Conclusion: AGEs and circulating RAGE are independently associated with haemoglobin and anaemia in older women. AGEs are amenable to interventions, as serum AGEs can be lowered by a change in dietary pattern and pharmacological treatment.

Keywords: *advanced glycation end products, anaemia, haemoglobin, women, elderly*

Anaemia is common in older adults, and the prevalence of anaemia increases with advancing age [1]. The factors that cause anaemia in older persons have not been completely characterised. Advanced glycation end products (AGES) are bioactive molecules implicated in the pathogenesis of renal insufficiency, diabetes and atherosclerosis [2]. AGEs are formed by the non-enzymatic glycation of proteins and other molecules. Recent studies suggest that AGEs accumulate in erythrocytes [3] and alter their deformability [4]. The decreased deformability induced by AGEs in erythrocytes is reversed by AGE inhibitors [4]. The AGEs on the surface of erythrocytes can bind with the receptor for AGEs (RAGE) on the vascular endothelium [5]. A previous study described elevated serum AGEs in anaemic patients with type 2 diabetes [6], but it is not clear whether elevated AGEs are associated with anaemia in the general population.

The two major sources of AGEs are exogenous AGEs ingested in foods and endogenous AGEs formed in the body. AGEs accumulate in tissues, and the rate accelerates with ageing [7]. The western diet is rich in AGEs, as AGEs are

formed when food is processed at elevated temperatures, i.e. deep frying, broiling and grilling [8]. About 10% of ingested AGEs are absorbed, and two-thirds of absorbed AGEs are retained in tissues [8]. In humans, lower dietary intake of AGEs reduces serum AGEs, decreases inflammation and improves vascular function [9]. AGE breakers or inhibitors improve arterial compliance, cardiac function and renal function in humans [2, 10].

AGEs upregulate inflammation through the receptor for AGEs (RAGE) located on the membrane of many types of cells [10]. Circulating isoforms of RAGE include endogenous secretory RAGE (esRAGE), a splice variant of RAGE that is secreted into blood and lacks the transmembrane and cytoplasmic portion of the receptor [11], and truncated forms of RAGE that have been cleaved from the cell surface by matrix metalloproteinases [10]. The relationship between circulating forms of RAGE and anaemia has not been characterised. There may be differences between concentrations of the two circulating receptors because esRAGE is expressed after transcriptional activation. Circulating RAGE can bind AGE and prevent AGE activation of cell membrane-bound RAGE [12]. Circulating RAGE may serve as a decoy receptor to counteract the inflammatory processes triggered by RAGE ligands such as AGEs [10]. Thus, in order to have greater insight into the role of AGEs and RAGE in relation to anaemia, both AGEs and RAGE should be considered.

The AGE–RAGE pathway has been the focus of growing interest because of substantial improvement in measurement technology and because experiments conducted in animal models have shown that blockage of AGE–RAGE binding may reduce the deleterious effects of AGEs on disease [10]. We postulated that elevated levels of serum AGE, sRAGE and esRAGE were associated with anaemia. To address this hypothesis, we characterised AGE, sRAGE and esRAGE and anaemia in a cohort of older women living in the community.

Materials and methods

Study population

Subjects in this study were women, aged 65 and older, who participated in the Women's Health and Aging Study I (WHAS I), a population-based study designed to evaluate the causes and course of physical disability in older disabled women living in the community. WHAS I participants were recruited from an age-stratified random sample of women aged 65 years and older selected from Medicare enrollees residing in 12 contiguous zip code areas in Baltimore [13]. Women were screened to identify self-reported physical disability that was categorised into four domains. The domains of disability were ascertained in a 20- to 30-min home interview that included questions related to (i) mobility and exercise tolerance, i.e. walking for a quarter of a mile, walking up 10 steps without resting, getting in and out of bed or chairs; (ii) upper extremity function, i.e. raising your arms up over your head, using your fingers to grasp or handle, lifting or carrying something as heavy as 10 pounds; (iii) higher functioning tasks (a subset of instrumental activities of daily living, not including heavy housework, i.e. using the telephone, doing light housework, preparing your own meals, shopping for personal items); and (iv) basic self-care tasks (a subset of non-mobility-dependent activities of daily living, i.e. bathing or showering, dressing, eating, using the toilet). WHAS I enrolled the one-third most disabled women ages 65 and older, those with disability in two or more domains. Of the 1,409 women who met study eligibility criteria, 1,002 agreed to participate in the study in 1992. There were no major differences in sociodemographic or reported health characteristics between eligible participants and those who declined to participate [13].

At the 12-month follow-up visit, 879 women returned for the follow-up, of which 580 received a blood draw. AGE and RAGE were measured in 519 women who had haemoglobin measurements available. The 519 women involved in the present study were significantly younger, and a higher proportion had MMSE score <24, level of education <12 years and stroke compared with the 360 women who are not included in the present analysis. Laboratory measurements of serum AGEs, sRAGE and esRAGE were done at the 12-month follow-up visit rather than at enrolment because of a greater availability of serum aliquots from this visit.

Data collection

Standardised questionnaires were administered in the participant's home by trained interviewers. Race was assessed in a questionnaire as black, white, or other, current smoking as yes or no and education as 0–8, 9–11, 12 or more than 12 years as the highest level of formal education achieved. Two weeks later, a trained registered full-time study nurse practitioner examined each study participant in her home, using a standardised evaluation of physical performance and physical exam. Approximately 75% of women also consented to phlebotomy performed during a separate visit by a trained phlebotomist who followed a standardised protocol. The definitions for the chronic diseases reported in this study were adjudicated by WHAS co-investigators based on standardised algorithms that combined information from the questionnaire, physical examination and physician contact [13]. The Mini-Mental Status Examination (MMSE) was administered at enrolment [13]. Further details on the methods and sampling design of the WHAS studies are published elsewhere [13]. The study protocol was adherent to the Declaration of Helsinki. The Johns Hopkins University Institutional Review Board approved the study protocol, and written informed consent was obtained from all participants.

Laboratory studies

Non-fasting blood samples were obtained by venipuncture between 9 AM and 2 PM. The blood samples were delivered to Quest Diagnostics Laboratories (formerly Ciba-Corning Laboratories, Baltimore, MD) on the day of blood drawing for complete blood count, folate, vitamin B_{12}, creatinine and serum iron measurements. Serum creatinine was measured

using the Jaffe method. Serum vitamin B_{12} and folate were measured by immunoassay [14]. Processing, aliquoting and freezing were carried out at the Core Genetics Laboratory of the Johns Hopkins University School of Medicine following a standardised protocol. The blood samples were stored continuously at −70°C until the time of analyses of serum AGEs, sRAGE and esRAGE.

The measure of serum AGEs in this study was serum carboxymethyl-lysine (CML). CML is a dominant circulating AGE, the best characterised of all the AGEs, and a dominant AGE in tissue proteins [15]. CML was measured using a competitive ELISA (AGE-CML ELISA, Microcoat, Penzberg, Germany) [16]. This assay has been validated [17], is specific and shows no cross-reactivity with other compounds [16]. Total sRAGE was measured using a sandwich ELISA (Quantikine Human RAGE Immunoassay, R&D Systems, Minneapolis, MN). This assay measures C-truncated RAGE that has been enzymatically cleaved from the cell surface as well as esRAGE. Serum esRAGE was measured using ELISA (B-Bridge International, Mountain View, CA) [18]. Measurements were all performed in duplicate according to the protocol of the manufacturers, and the results were averaged. The within-assay and between-assay coefficients of variation (CVs) for serum CML, sRAGE and esRAGE were 3% and 4%, 3% and 7% and 6% and 8%, respectively.

Statistical analysis

Continuous variables were compared using the Wilcoxon rank-sum test. Categorical variables were compared using chi-square tests. Anaemia was defined as haemoglobin <12 g/dL. Types of anaemia were defined using a framework previously described [19]. In brief, among women with haemoglobin <12 g/dL, iron deficiency anaemia was defined as serum ferritin <12 mg/L, folate deficiency anaemia was defined as serum folate <5.89 nmol/L and anaemia due to serum vitamin B_{12} deficiency was defined as serum vitamin B_{12} <200 pg/mL. Among anaemic women, the anaemia of chronic inflammation was defined as serum iron <60 μg/dL and serum ferritin >12 mg/L, and anaemia due to renal disease was defined as anaemia in the presence of an estimated glomerular filtration rate of <30 mL/min/1.73 m^2. Unexplained anaemia was defined as anaemia that was not due to iron, folate or vitamin B_{12} deficiencies, or due to the anaemia of chronic inflammation or renal disease.

Body mass index (BMI) was categorised as underweight (<18.5 kg/m^2), normal range (18.5–24.9 kg/m^2), overweight (≥25–29.9 kg/m^2) and obese (≥30 kg/m^2) [19]. A MMSE score of <24 was defined as cognitive impairment [13]. Renal insufficiency was defined as an estimated glomerular filtration rate of <60 mL/min/1.73 m^2 using the Modification of Diet in Renal Disease equation of Levey and colleagues [20]. Logistic regression models were used to examine separately the relationships of serum CML, sRAGE and esRAGE with anaemia. Linear regression models were used to examine the same cross-sectional relationships where the dependent variable was haemoglobin. Variables that were significant in the univariate analyses were entered into the multivariate logistic and linear regression models. In linear and logistic regression models, a one standard deviation (SD) in the concentration of serum CML, sRAGE and esRAGE, respectively, was used as the unit of change. The statistical program used was SAS (SAS Institute, Cary, NC), with data analysis conducted by Kai Sun. The level of significance used in this study was $P < 0.05$.

Results

The demographic and health characteristics of 519 women with and without anaemia are shown in Table 1. Of the 519 women, 128 (24.7%) had anaemia. Women with anaemia were more likely to be non-white, have a lower level of education, MMSE score <24 and to have hypertension, diabetes and renal insufficiency and less likely to be current smokers or to have chronic obstructive pulmonary disease. There were no significant differences in age, body mass index, angina, congestive heart failure, peripheral artery disease, stroke, depression or cancer between women with and without anaemia. Median serum CML concentrations were significantly higher in women with anaemia compared to women without anaemia, whereas median serum sRAGE and esRAGE levels were not significantly different between groups ($P = 0.14$, $P = 0.06$, respectively). There were 41 women who were taking hormonal replacement therapy. Among women who were or were not taking hormonal replacement therapy, mean (SD) serum CML, sRAGE and esRAGE concentrations were 0.60 (0.16) and 0.58 (0.19) μg/mL ($P = 0.19$), 1.27 (0.74) and 1.36 (0.71) ng/mL ($P = 0.33$) and 0.36 (0.25) and 0.38 (0.21) ng/mL ($P = 0.25$), respectively.

Separate multivariate logistic regression models were used first to examine the cross-sectional relationship between serum CML, sRAGE and esRAGE with anaemia (Table 2). Serum CML, sRAGE and esRAGE (per 1 SD increase), respectively, were associated with anaemia in separate multivariate logistic regression models adjusting for age; for age, race, smoking and education; and for age, race, smoking, education, MMSE score, hypertension, diabetes, chronic obstructive pulmonary disease and renal insufficiency.

Serum CML, sRAGE and esRAGE (per 1 SD increase), respectively, were inversely associated with haemoglobin in separate multivariate linear regression models adjusting for age; for age, race, smoking and education; and for age, race, smoking, education, MMSE score, hypertension, diabetes, chronic obstructive pulmonary disease and renal insufficiency (Table 3).

In an additional set of analyses, we excluded all women who were diabetic. Serum CML, sRAGE and esRAGE (per 1 SD increase), respectively, were associated with anaemia in separate multivariate logistic regression models (OR 1.29, 95% CI 1.01–1.64, $P = 0.04$; OR 1.47, 95% CI 1.14–1.91, $P = 0.003$; OR 1.34, 95% CI 1.05–1.73, $P = 0.02$), adjusting for age, race, smoking education, MMSE score, hypertension, chronic obstructive pulmonary disease and

Table 1. Demographic and health characteristics of women, aged ≥65 years, in the Women's Health and Aging Study I in Baltimore, MD, with and without anaemia

		Anaemic ($n = 128$)		Not anaemic ($n = 391$)		
Characteristics[a]		*n*	% or median (25th, 75th percentile)	*n*	% or median (25th, 75th percentile)	*P*
Age (years)		128	77.0 (71.0, 84.5)	391	75.0 (70.0, 83.0)	0.12
Race	White	65	50.8	301	77.0	<0.0001
	Other	63	49.2	90	23.0	
Education <12 years		90	70.9	233	59.7	0.02
Current smoker		7	5.5	50	12.8	0.03
Body mass index (kg/m^2)	<18.5	5	4.3	11	3.1	0.36
	18.5–24.9	22	18.8	95	26.8	
	25.0–29.9	44	37.6	119	33.6	
	≥30	46	39.3	129	36.4	
Serum CML (μg/mL)		128	0.59 (0.46, 0.76)	387	0.54 (0.44, 0.65)	0.0018
Serum sRAGE (ng/mL)		127	1.26 (0.89, 1.93)	385	1.20 (0.86, 1.63)	0.14
Serum esRAGE (ng/mL)		127	0.38 (0.25, 0.50)	391	0.34 (0.24, 0.44)	0.06
Mini-Mental Status Exam score <24 (%)		29	22.7	51	13.0	0.03
Hypertension (%)		87	68.0	213	54.6	0.008
Angina (%)		25	19.5	87	22.2	0.52
Congestive heart failure (%)		16	12.5	32	8.2	0.14
Peripheral artery disease (%)		35	27.3	69	17.7	0.17
Stroke (%)		7	5.5	17	4.4	0.6
Diabetes mellitus (%)		33	25.8	45	11.5	<0.0001
Chronic obstructive pulmonary disease (%)		23	18.0	12	32.7	0.001
Depression (%)		22	17.2	53	13.6	0.31
Cancer (%)		13	10.2	47	12.0	0.56
Renal insufficiency (%)		77	60.2	191	49.1	0.03

[a]Median (25th, 75th percentile) for continuous variables or percent of participants with specific characteristic as noted.

Table 2. Multivariate logistic regression models of the relationship of serum CML, sRAGE and esRAGE with anaemia in women, aged ≥65 years, in the Women's Health and Aging Study I in Baltimore, MD[a]

	Model adjusted for age			Model adjusted for age, race, smoking, education			Model adjusted for age, race, smoking, education, MMSE, chronic diseases[c]		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Serum CML[b] (μg/mL)	1.51	1.16–1.95	0.0018	1.50	1.15–1.97	0.003	1.47	1.11–1.95	0.008
Serum sRAGE[b] (ng/mL)	1.25	1.03–1.52	0.026	1.58	1.26–1.97	<0.0001	1.52	1.21–1.92	0.0004
Serum esRAGE[b] (ng/mL)	1.22	1.01–1.47	0.048	1.56	1.24–1.94	<0.0001	1.49	1.18–1.87	0.0006

[a]Separate logistic regression models shown for serum CML, sRAGE and esRAGE in which anaemia is the dependent variable.
[b]Odds ratios are expressed per 1 SD change in serum CML, sRAGE and esRAGE, respectively.
[c]Chronic diseases were hypertension, diabetes, chronic obstructive pulmonary disease and renal insufficiency.

Table 3. Multivariate linear regression models of the relationship of serum CML, sRAGE and esRAGE at baseline with haemoglobin in women, aged ≥65 years, in the Women's Health and Aging Study I in Baltimore, MD[a]

	Model adjusted for age			Model adjusted for age, race, smoking, education			Model adjusted for age, race, smoking, education, MMSE, chronic diseases[c]		
	Beta	SE	*P*	Beta	SE	*P*	Beta	SE	*P*
Serum CML[b] (μg/mL)	−0.19	0.06	0.001	−0.17	0.06	0.003	−0.17	0.06	0.004
Serum sRAGE[b] (ng/mL)	−0.15	0.06	0.018	−0.29	0.06	<0.0001	−0.27	0.06	<0.0001
Serum esRAGE[b] (ng/mL)	−0.16	0.06	0.01	−0.31	0.06	<0.0001	−0.30	0.06	<0.0001

[a]Separate linear regression models shown for serum CML, sRAGE and esRAGE in which haemoglobin is the dependent variable.
[b]Betas are expressed per 1 SD change in serum CML, sRAGE and esRAGE, respectively.
[c]Chronic diseases were hypertension, diabetes, chronic obstructive pulmonary disease and renal insufficiency.

Table 4. Serum CML, sRAGE, esRAGE and other characteristics of women without anaemia and with specific types of anaemia in the Women's Health and Aging Study I

Characteristics	Non-anaemic ($n = 399$)	Anaemic with nutrient deficiency[a] ($n = 25$)	Anaemia of chronic inflammation[b] ($n = 55$)	Anaemic with renal disease[c] ($n = 7$)	Unexplained anaemia[d] ($n = 48$)	*P*
Age (years)	75.0 (70.0, 83.0)	75.5 (72.0, 85.0)	76.0 (70.0, 84.0)	73.0 (70.0, 84.0)	79.0 (72.0, 86.0)	0.38
Black race (%)	23.0	62.5	50.0	57.1	39.5	<0.0001
Education <12 years (%)	59.7	83.3	67.9	71.4	67.4	0.13
Current smoker (%)	12.8	12.5	7.4	0	0	0.05
Serum CML (μg/mL)	0.54 (0.44, 0.65)	0.54 (0.44, 0.71)	0.58 (0.47, 0.73)	0.85 (0.60, 1.89)	0.60 (0.46, 0.78)	0.002
Serum sRAGE (ng/mL)	1.20 (0.86, 1.64)	0.95 (0.69, 1.74)	1.29 (0.94, 1.89)	2.12 (1.84, 3.66)	1.21 (0.95, 1.72)	0.007
Serum esRAGE (ng/mL)	0.34 (0.24, 0.44)	0.26 (0.17, 0.42)	0.40 (0.27, 0.50)	0.53 (0.45, 0.58)	0.39 (0.26, 0.57)	0.005
Mini-Mental Status Exam score <24 (%)	13.0	12.5	31.5	14.3	18.6	0.02
Hypertension (%)	54.6	66.7	68.5	71.4	67.4	0.13
Angina (%)	22.2	20.8	14.8	28.6	23.3	0.76
Congestive heart failure (%)	8.2	25.0	5.6	0	16.3	0.02
Peripheral artery disease (%)	17.6	20.8	22.2	57.1	32.6	0.02
Stroke (%)	4.3	4.2	5.6	0	6.9	0.89
Diabetes (%)	11.5	25.0	25.9	28.6	25.6	0.003
Chronic obstructive pulmonary disease (%)	32.7	20.8	22.2	14.3	11.6	0.02
Depression (%)	13.6	12.5	20.4	14.3	16.3	0.74
Cancer (%)	12.0	12.5	9.3	0	11.6	0.87

[a]Anaemic with nutritional deficiency defined as anaemia with either serum ferritin <12 mg/L, serum folate <5.89 nmol/L and/or serum vitamin B_{12} <200 pg/mL.
[b]Anaemia of chronic inflammation defined as anaemia with serum iron <60 μg/dL and serum ferritin >12 mg/L.
[c]Anaemia due to renal disease was defined as anaemia with an estimated glomerular filtration rate of <30 mL/min/1.73 m^2.
[d]Unexplained anaemia was defined as anaemia that was not due to iron, folate or vitamin B_{12} deficiencies or due to the anaemia of chronic inflammation or renal disease.

renal insufficiency. Serum CML, sRAGE and esRAGE (per 1 SD increase), respectively, were inversely associated with haemoglobin in separate multivariate linear regression models (beta = −0.19, SE = 0.06, $P = 0.0018$; beta = −0.29, SE = 0.06, $P < 0.0001$; beta = −0.26, SE = 0.06, $P < 0.0001$) adjusting for age, race, smoking education, MMSE score, hypertension, chronic obstructive pulmonary disease and renal insufficiency.

Median serum CML, sRAGE and esRAGE concentrations in different types of anaemia are shown in Table 4. Serum CML concentrations were highest in women with anaemia, with renal disease and unexplained anaemia. Median serum sRAGE and esRAGE concentrations were highest in women with anaemia of chronic inflammation, anaemia with renal disease and unexplained anaemia.

Discussion

The present study suggests that elevated AGEs, as indicated by serum CML, are inversely associated with haemoglobin and directly associated with anaemia in older, community-dwelling women. To our knowledge, this is the first study to report an association between elevated AGEs and anaemia in a population of community-dwelling adults. The present study is consistent with a previously reported association of elevated AGEs and anaemia among patients with type 2 diabetes [6], and it extends these findings, as the association between AGEs and anaemia was also consistent among patients without diabetes. The present study also adds to what is known about AGEs and anaemia by showing the relationship between elevated circulating RAGE and anaemia. As noted previously, AGEs alter the deformability of erythrocytes and increase interactions between erythrocytes and the endothelial surface via interactions of erythrocyte AGE with RAGE [3–5]. In addition, CML forms adducts with haemoglobin [21], but whether the formation of haemoglobin–CML affects the lifespan of erythrocytes or contributes to anaemia via other biological mechanisms should be examined in future studies.

Serum CML, sRAGE and esRAGE concentrations appear to be the highest in women with renal disease compared with women who had other types of anaemia or were non-anaemic. Elevated serum or plasma AGEs have previously been described in patients with diabetic nephropathy [22] and end-stage renal disease [23]. AGEs can contribute to chronic kidney disease by inducing glomerulosclerosis and interstitial fibrosis [24]. The progression of chronic kidney disease can contribute to elevated systemic levels of AGEs, thus worsening a vicious cycle. The relationship between AGEs, chronic kidney disease and anaemia needs to be expanded in future studies, as patients with chronic kidney disease may be at the highest risk of elevated AGEs and anaemia. Elevated circulating RAGE has been described in patients with end-stage renal disease [25].

The present study showed that sRAGE and esRAGE were elevated in anaemic compared with non-anaemic women. It should be noted that the relationships of sRAGE and esRAGE with chronic diseases have been inconsistent in the literature. For example, studies have reported either higher or lower sRAGE concentrations in patients with diabetes or in patients with coronary artery disease compared with controls [10]. Similarly, both higher and lower circulating

esRAGE concentrations have been associated with diabetes and coronary artery disease [10]. Further studies will be needed to determine whether elevated sRAGE and esRAGE are associated with anaemia in other populations.

This study has some limitations. Because of the cross-sectional, correlational nature of this study, whether there is a causal relationship between elevated serum CML and anaemia is not clear. The study did not include any nutritional assessment or the dietary assessment of AGEs, which must be conducted using a specialised questionnaire that addresses the method of food preparation. However, serum CML concentrations have been shown previously to correlate well with dietary intake of AGEs [26, 27]. The study was conducted in moderately to severely disabled older women, and the findings cannot necessarily be extrapolated to less disabled women or to older men.

Serum AGEs are a potentially modifiable risk factor, as systemic levels of AGEs can be reduced substantially by decreasing dietary intake of AGEs by avoiding foods that are processed at high temperatures, i.e. deep fried, oven fried, grilled and broiled [9]. Administration of AGE breakers or AGE inhibitors has been shown to improve reduce endothelial dysfunction and to improve cardiovascular and renal function [28–30], but it is not known whether these pharmacological or dietary interventions will affect haemoglobin concentrations.

In conclusion, elevated CML, a dominant AGE, is independently associated with anaemia in older, moderately to severely disabled community-dwelling women. Further epidemiological studies are needed to determine whether elevated AGEs and circulating RAGE predict the development of anaemia. Clinical studies are needed to determine whether AGEs influence the fragility or lifespan of erythrocytes. AGEs could be a potential target for interventions to prevent onset as well as progression of anaemia, as serum AGEs can be lowered by a change in dietary pattern and pharmacological treatment.

Key points

- Advanced glycation end products (AGEs) are known to accumulate in erythrocytes in circulation and affect their deformability, but it is unclear whether older adults with elevated serum AGEs are at higher risk of anaemia.
- Population-based study of older women living in the community examining relationship of serum AGEs and circulating receptors for AGEs (RAGE) with haemoglobin and anaemia.
- Elevated serum AGEs and RAGE are independently associated with anaemia and haemoglobin among older women living in the community.

Acknowledgements

This work was supported by National Institute on Aging Grant R01 AG029148, R01 AG027012, R37 AG19905, and the Intramural Research Program, National Institute on Aging, NIH.

Conflicts of interest

None.

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Received 5 June 2008; accepted in revised form 4 December 2008