Serum sclerostin as a potential biomarker of vascular and valvular types of calcification in chronic kidney disease cases with and without maintenance hemodialysis

Thanaa Fathi Moghazy, Moyassar Ahmad Zaki, Noha Said Kandil, Dalia Aly Maharem, Khaled Aly Matrawy, Moataz Ahmad Zaki and Alaa Mohamed Ismail El-Banna

Medical Research Institute, Alexandria University, Alexandria, Egypt

ABSTRACT

**Introduction:** Vascular calcification (VC) is one of the factors involved in the increased cardiovascular risk observed in chronic kidney disease. Sclerostin is known to be a down regulator of bone mineralization, and a potential molecule linking the bone-vascular axis. The present study aimed at measuring serum sclerostin level in both dialyzed and undialyzed cases and correlating its serum level with both vascular and valvular types of calcification.

**Methods:** This case control study was conducted on 82 Egyptian subjects of comparable age and gender divided into 20 apparently healthy volunteers as well as 62 chronic kidney disease cases of whom 31 cases were under maintenance hemodialysis (HD) for more than 6 months. Serum sclerostin was measured using an enzyme immunoassay.

**Results:** Significantly higher median serum sclerostin values were observed in each of dialyzed and undialyzed cases compared to each others and to control group. Serum sclerostin was positively correlated with old age, male gender, and VC in dialyzed cases, and inversely correlated with estimated glomerular filtration rate in total number of cases. Diagnostic performance of serum sclerostin revealed a sensitive rather than a specific biomarker of both vascular and valvular types of calcification. Multiple regression analysis revealed an independent contribution of male gender, estimated glomerular filtration rate, and valvular calcification to serum sclerostin level.

**Conclusion:** Serum sclerostin level could be used as a potential biomarker for both vascular and valvular types of calcification in chronic kidney disease cases regardless maintenance HD as a treatment modality.

1. Introduction

Cardiovascular (CV) complications, account for 50% of deaths in end stage renal disease (ESRD) patients. Increased vascular calcification (VC) in chronic kidney disease (CKD) patients predicts a poor prognosis in overall survival and CV morbidity and mortality [1]. Measurement of carotid artery intima media thickness (CIMT) is commonly used to assess the degree of atherosclerosis that occurs in 50% of CKD patients not yet on dialysis and in 70–90% of dialyzed patients [2].

It is well established that the process of VC is controlled by a balance between pro-calcifying and anti-calcifying regulatory proteins acting locally in the vessel wall and/or systemically in the circulation [1,3]. The pathogenesis of VC in CKD results from an active process of transformation of vascular smooth muscle cells (VSMCs) into osteoblast-like cells [1,4]. Radiological means for the detection of vascular and valvular types of calcification that associate CV complications remain the gold standard, yet several biomarkers are being studied among which sclerostin is a potential one.

Sclerostin is a 190 amino acid residue glycoprotein, with a molecular mass of 24 kilo daltons and a sequence homology similar to that of other bone morphogenetic protein antagonists. The central core of sclerostin comprises the C-terminal cystine knot domain and three loop regions, with loops 1 and 3 having twisted antiparallel β-sheets that form finger-like structures, whereas loop 2 is critical for the binding of sclerostin to the low-density-lipoprotein-related protein (LRP) 5/6 coreceptors [5].

Sclerostin exerts its anti-anabolic effects in bone, namely inhibition of bone formation and mass, via competing with wingless Int (Wnt) ligand for binding to the LRP 5/6 coreceptors at the cell surface causing the unphosphorylation of cytoplasmic tail of LRP 5/6, and hence axin does not bind the receptor complex [5,6]. This will result in an uninterrupted glycogen synthase kinase-3β activity and hence phosphorylation of β-catenin, targeting it for degradation. The low cytosolic β-catenin level prevents its translocation to the nucleus thus causing inactivation of target gene promoters of the Wnt signaling pathway [5,6].

CONTACT Noha Said Kandil dtnohakandili@yahoo.com; nohakandil@gmail.com Chemical Pathology Department, Medical Research Institute, Alexandria University, 165 El-Horreya Avenue – El-Hadara, Alexandria 21561, Egypt © 2019 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
Emerging experimental evidence suggests that some inhibitors of the canonical Wnt signaling pathway, which is actively involved in bone formation and VC, play a role linking VC and bone [3,4,6]. Vascular smooth muscles cells (VSMCs) undergo osteo/chondrogenic trans-differentiation in a pro-calcifying environment. The resulting osteoblast-like cells induce alkaline phosphatase (ALP) activity, responsible for the vascular tissue mineralization process [1,4]. Sclerostin is usually expressed in the late phase of VC, yet its role in the process of VC is still controversial.

Several physiological factors increase circulating sclerostin level including old age [7], male gender [7], as well as seasonal variation [8], being higher in fall than in winter. On the other hand, serum sclerostin level was reported to be elevated in obesity [9], hypoparathyroidism [10], CKD [3,11], osteoporosis [12], type-2 diabetes mellitus [13], in response to some drugs as well as cytokines and growth factors such as tumor necrosis factor-α and bone morphogenetic proteins [11].

As the exact role of sclerostin, particularly its serum level, in the process of VC remains unclear, it was noteworthy to study its serum level in both dialyzed and non-dialyzed CKD patients as a potential predictor of both vascular and valvular types of calcification.

2. Subjects

This case control study was conducted in the Medical Research Institute Teaching hospital starting from October till December of the year 2017. Informed consents were obtained from the 82 participants enrolled in this study. The study was approved by the Institute’s ethical committee and was in concordance with the Helsinki Declaration of 1975, as revised in 2000. Participants were divided into 20 apparently healthy volunteers and 62 CKD cases with CKD being defined by renal injury detected by radiological, pathological, or biochemical methods for 3 months and/or a glomerular filtration rate (GFR) less than 60mL/min for 3 months, of whom 31 cases being end stage renal disease (ESRD) undergoing maintenance hemodialysis (HD). All subjects were screened for diabetes according to the American Diabetes Association (ADA) criteria using random serum glucose. Following an overnight fasting period, 5 mL of whole venous blood were obtained from each subject. Blood from HD patients was drawn immediately before the dialysis session. The serum obtained following centrifugation was divided into three portions; one portion was used for measuring levels of creatinine, uric acid, cholesterol and its high density fraction, triglycerides, calcium, phosphorus, albumin, and activities of aminotransferases, gamma glutamyl transferase, and alkaline phosphatase with analyses being conducted on the Olympus AU400 clinical chemistry analyzer (Beckman Coulter Inc., Brea CA, USA). The other portion was used for the determination of intact parathormone level using an electrochemiluminescent immunoassay on the e601 module of the cobas 6000 modular analytical platform (Roche Diagnostics, Mannheim, Germany). The last portion was stored at -20°C till the time of assay of serum sclerostin level.

3. Methods

3.1. Clinical examination and anthropometric measurements

To all participants, full history taking was done, with stress on drug history, as well as the duration of disease in CKD cases and duration of dialysis in ESRD cases. Anthropometric measurements, namely body weight, height, and triceps skin fold (TSF), were done along with calculations of body mass index (BMI), total body water (TBW), total body fat (TFB), and fat free mass (FFM).

3.2. Radiological investigations

Documentation of VC in CKD cases was done using a B-mode ultrasonography of the common carotid arteries [14]. In addition carotid intima media thickness was measured using the same B-mode ultrasound [14].

3.3. Echocardiographic assessment

Mitral or aortic annular calcification in CKD cases was detected by transthoracic echocardiography of the cardiac valves using a commercial Philips HD 7 with a 3-MHz probe. Calcification thickness greater than 1 mm and less than 4 mm was considered mild to moderate, and greater than 4 mm was considered severe [15].

3.4. Laboratory investigations

All subjects were screened for diabetes according to the American Diabetes Association (ADA) criteria using random serum glucose. Following an overnight fasting period, 5 mL of whole venous blood were obtained from each subject. Blood from HD patients was drawn immediately before the dialysis session. The serum obtained following centrifugation was divided into three portions; one portion was used for measuring levels of creatinine, uric acid, cholesterol and its high density fraction, triglycerides, calcium, phosphorus, albumin, and activities of aminotransferases, gamma glutamyl transferase, and alkaline phosphatase with analyses being conducted on the Olympus AU400 clinical chemistry analyzer (Beckman Coulter Inc., Brea CA, USA). The other portion was used for the determination of intact parathormone level using an electrochemiluminescent immunoassay on the e601 module of the cobas 6000 modular analytical platform (Roche Diagnostics, Mannheim, Germany). The last portion was stored at -20°C till the time of assay of serum sclerostin level. Calculations of estimated glomerular filtration rate (eGFR) using the Cockcroft and Gault formula, low-density fraction of cholesterol using the Friedewald formula and calcium phosphate solubility product were also done.

Serum sclerostin level was determined using a human type enzyme labelled immunoassay (lot No. wp 161, CAT No. BI-20492, Biomedica Medizinprodukte GmbH & Co KG, A-1210, Wien, Austria) according to the manufacturer’s instructions. The assay had an intra- and inter- assay percent coefficients of variation of less than 7% and 10%, respectively. Furthermore, no cross reactivity with Wise (SOSTDC1) or noggin, nor with rat or mouse sclerostin was declared.
by the manufacturer. The lower limit of quantification for this assay was 7.5 pmol/L.

3.5. Statistical analysis

Data analysis was performed using Statistical Package of Social Science (SPSS) for Windows, version 20 (SPSS, Inc., Chicago, IL). Chi-square test was used for gender comparison. Categorical data were presented as percentages. Kolmogorov–Smirnov test of normality was done to determine the distribution of data. Descriptive statistics namely mean and standard deviation for parametric data, or median and range for non-parametric data were done. Comparison between groups was done using ANOVA and independent samples t-test for parametric data, or Kruskal–Wallis and Mann–Whitney tests for nonparametric data. Spearman rank correlation studies were used to test for the degree of association between variables. Receiver Operating Characteristics (ROC) curve analysis was used to obtain the best cut off values for serum sclerostin as a potential marker of vascular and valvular calcification. Multiple linear regression analysis was carried out to analyze the relationship between a dependant variable and several other anticipated independent predictor variables. A p-value less than 0.05 was considered statistically significant.

4. Results

The demographical characteristics shown in this study are summarized in Table 1. The duration of kidney disease in non-dialyzed cases ranged from 1 to 10 years with a median value of 4 years, while in dialyzed cases the duration of dialysis ranged from 3 to 12 years with a median value of 5 years (Table 1). Significantly lower BMI, TBW, FFM, and TBF values, together with a significantly higher TSF value were noted in dialyzed cases compared to non-dialyzed cases. Moreover, a significantly higher TSF value was noted in dialyzed cases compared to the control group (Table 2).

Ultrasonographic evidence of VC was detected in 35.5% of dialyzed cases and in 9.7% of non-dialyzed cases (Table 2) (Figure 1), while echocardiographic evidence of valvular calcification was detected in 74.2% of dialyzed cases and 38.8% of non-dialyzed cases (Table 2) (Figure 2). The CIMT values in both dialyzed and non-dialyzed cases were significantly higher than its value in the control group. When a CIMT cutoff value of 0.8 mm was chosen, 77.4% of dialyzed, and 58.1% of non-dialyzed cases had a value of ≥0.8 mm (Table 2).

Serum creatinine level in the present study was significantly higher in dialyzed cases compared to non-dialyzed cases and controls which is consistent with the degree of renal impairment (Table 3). Furthermore, the value for the eGFR in the undialyzed cases ranged from 16.2 to 59.8 mL/min corresponding to stages 3 and 4 of CKD (Table 3). Estimated GFR showed lowest median value in dialyzed cases, followed by non-dialyzed cases and finally a within reference interval eGFR for the control group (Table 3).

Significantly high calcium phosphate solubility product and intact parathormone values were

| Age (years) | Control group (n = 20) | Non-dialyzed CKD group (n = 31) | Dialyzed CKD group (n = 31) | Test of sig. | p-value |
|------------|-----------------------|-------------------------------|-----------------------------|--------------|---------|
| 20–30      | 1 5.0                 | 2 6.5                         | 3 9.7                      | χ² = 6.785   | MC p = 0.570 |
| 31–40      | 5 25.0                | 4 12.9                        | 7 22.6                     |              |         |
| 41–50      | 10 50.0               | 13 41.9                       | 15 48.4                    |              |         |
| 51–60      | 4 20.0                | 7 22.6                        | 3 9.7                      |              |         |
| >60        | 0 0.0                 | 5 16.1                        | 3 9.7                      |              |         |
| <45        | 12 38.7               | 8 25.8                        | 9 45.0                     | χ² = 2.203   | 0.332   |
| ≥45        | 19 61.3               | 23 74.2                       | 11 55.0                    |              |         |
| Mean ± SD. | 44.23 ± 10.11         | 48.68 ± 10.11                 | 45.15 ± 8.41               | F = 1.759    | 0.179   |

Gender

| Control group (n = 20) | Non-dialyzed CKD group (n = 31) | Dialyzed CKD group (n = 31) | Test of sig. | p-value |
|-----------------------|-------------------------------|-----------------------------|--------------|---------|
| Female                | 11 55.0                       | 16 51.6                     | 15 48.4      | χ² = 0.216 | MC p = 0.898 |
| Male                  | 9 45.0                        | 15 48.4                     | 16 51.6      |         |

χ²: χ² for Chi-square test.
p: p value for comparing between the three studied groups.
MC: Monte Carlo for Chi-square test for comparing between the three groups.
F: F-value for ANOVA test.
observed in CKD cases whether dialyzed or not compared to each other as well as to control group (Table 3). At a cutoff value of 55 mg²/dL², 9 out to 31 (29%) dialyzed cases and 3 out of 31 (9.7%) non-dialyzed cases had a serum calcium phosphate product ≥ 55 mg²/dL² (Table 3).

Lowest serum albumin was evident in non-dialyzed cases followed by dialyzed cases when compared to the control group. Serum ALP activity had the highest median value in dialyzed cases compared to both undialyzed cases and control group (Table 3). As regards the parameters reflecting lipid metabolism, hypertriglyceridemia was observed in dialyzed and undialyzed cases compared to the control group. Despite within accepted reference intervals for serum total cholesterol, yet disturbances in its low- and high-density fractions (higher median values in the former and lower median values in the latter in both patient groups) were also noted in both groups of patients compared to the control group (Table 3).
Serum sclerostin median value showed a statistically significant difference among the three studied groups, with highest median value observed in dialyzed cases, followed by non-dialyzed cases and finally control group (Figure 3). Furthermore, serum sclerostin median value was significantly higher in dialyzed cases ≥45 years compared to dialyzed cases <45 years ($p = 0.039^*$). As regard gender, higher median values for serum sclerostin were observed in males compared to females in all CKD cases ($p = 0.046^*$) as well as in undialyzed cases ($p = 0.006^*$). Significant positive correlations existed between serum sclerostin level and age in both dialyzed ($r = 0.426, p = 0.017^*$) and undialyzed ($r = 0.410, p = 0.022^*$) cases, as well as valvular calcification in both groups too ($r = 0.420, p = 0.019^*$ in dialyzed cases and $r = 0.644, p < 0.001^*$ in undialyzed cases, respectively), while a significant inverse relation was shown with eGFR in all cases regardless of dialysis ($r = −0.446, p < 0.001^*$).

The diagnostic performance of serum sclerostin as a potential biomarker of vascular and valvular types of calcification in all CKD cases was addressed in this study. Using the available radiological means for defining the type of calcification, ROC curve analysis was done generating cutoff values for serum sclerostin of 43.41 pmol/L for the vascular type (AUC = 0.720, $p = 0.013$) (Figure 4) and 39.47 pmol/L for the valvular type (AUC = 0.770, $p < 0.001$) (Figure 5) of calcification. Based on such cut off values, the diagnostic performance of serum sclerostin as a potential biomarker of VC revealed a sensitivity of 71.43% and a specificity of 56.25%, while its performance as a potential biomarker of valvular calcification revealed a sensitivity of 82.3% and a specificity of 63%.

The multiple linear regression analysis revealed that gender, valvular calcification, and eGFR as an indicator of renal pathology acted as independent variables that could influence serum sclerostin level.
Table 3. Serum levels and activities of selected biochemical parameters and calculations done among the studied groups.

| Items                        | Units            | Control group (n = 20) | Non-dialyzed group (n = 31) | Dialyzed group (n = 31) | Test of sig | p-value     |
|------------------------------|------------------|------------------------|-----------------------------|-------------------------|-------------|-------------|
| Glucose (Random)             | mg/dL            | 87.35 ± 7.51           | 91.81 ± 5.17                | 100.61 ± 16.73          | F = 9.186*  | <0.001*     |
| Creatinine                   | mg/dL            | 0.8 (0.5–0.9)          | 2.1 (1.4–6.1)               | 9.4 (6.2–14.0)          | H = 71.173* | <0.001*     |
| Estimated GFR                | mL/min           | 110 (100–161)          | 44.9 (16.2–59.8)            | 8.9 (5.1–14.9)          | H = 71.083* | <0.001*     |
| Cholesterol                  | mg/dL            | 150.45 ± 10.56         | 183.26 ± 73.11              | 155.29 ± 41.51          | F = 3.225*  | 0.045*      |
| HDL-Cholesterol              | mg/dL            | 49.0 (45.0–67.0)       | 23.0 (7.0–76.0)             | 18.0 (11.0–47.0)        | H = 40.695* | <0.001*     |
| LDL-Cholesterol              | mg/dL            | 83.4 ± 9.74            | 128.23 ± 54.17              | 106 ± 45.52             | F = 4.920*  | 0.010*      |
| Triglycerides                | mg/dL            | 81.25 ± 14.76          | 149.45 ± 56.76              | 145.42 ± 62.16          | F = 12.120* | <0.001*     |
| Albumin                      | gm/dL            | 4.5 ± 0.37             | 2.50 ± 0.86                 | 3.61 ± 0.87             | t = 5.036*  | <0.001*     |
| ALT                          | U/L              | 15 (10–20)             | 15 (7–77)                   | 16 (6–52)               | H = 0.479   | 0.787       |
| AST                          | U/L              | 13 (7–27)              | 18 (12–32)                  | 17 (12–25)              | H = 29.220* | <0.001*     |
| γGT                          | U/L              | 18 (10–23)             | 23 (8–81)                   | 25 (10–221)             | H = 13.966* | <0.001*     |
| ALP                          | U/L              | 58 (39–88)             | 73 (8–167)                  | 162 (49–739)            | H = 33.465* | <0.001*     |
| Calcium (Ca)                 | mg/dL            | 9.22 ± 0.39            | 9.43 ± 0.83                 | 9.02 ± 0.94             | F = 2.035   | 0.137       |
| Phosphorus (Pi)              | mg/dL            | 3.35 ± 0.43            | 4.44 ± 1.40                 | 5.22 ± 2.10             | F = 8.652*  | <0.001*     |
| Ca x Pi product              | mg²/dL²          | 30.88 ± 4.11           | 41.5 ± 12.42                | 47.3 ± 20.03            | F = 7.651*  | 0.001*      |
| Intact PTH                   | pg/mL            | 26.8 (19.0–33.0)       | 46.8 (10.0–150.7)           | 489.0 (28.9–2624)       | H = 53.096* | <0.001*     |

ALP: Alkaline phosphatase, ALT: Alanine aminotransferase, AST: aspartate aminotransferase, HDL: High density lipoprotein, γGT: Gamma glutamyl transferase, LDL: Low density lipoprotein, PTH: Parathormone.

in all CKD cases (n = 62) whether dialyzed or not (Table 4).

5. Discussion

In this case control study serum sclerostin was evaluated as a potential biomarker of vascular and valvular types of calcification in dialyzed and undialyzed cases. The commercial enzyme immunoassay used to measure serum sclerostin in this study was similar to that used by McNulty et al. [16], Ishimura et al. [17], and Kanbay et al. [18], thus reducing the potential influence of analytical factors on its serum level. A significantly higher serum sclerostin median value was noted among each of dialyzed and non-dialyzed cases compared to each other and to the control group (Figure 3). Several studies have demonstrated that serum
Figure 3. Serum sclerostin level (pmol/L) among the studied groups.

Figure 4. ROC curve analysis of serum sclerostin as a potential biomarker of carotid calcification in whole patients (n = 62).

Figure 5. ROC curve analysis of serum sclerostin as a potential biomarker of valvular calcification in whole patients (n = 62).
sclerostin level increases with CKD even in early stages [19,20]. The exact mechanism is still not quite clear whether it is due to decreased excretion or increased production as a reaction of the osteocyte to kidney injury, which is a part of the CKD-mineral bone disorder [21]. In that context, sclerostin expression was suggested as a defensive response that aims to block the Wnt signaling pathway in order to reduce the mineralization in the vascular tissue, where it may spill over to the circulation acting systemically to inhibit bone metabolism [3]. In our study, dialyzed cases aged 45 years or more showed a significantly higher serum sclerostin level compared to dialyzed cases less than 45 years of age. This was also evident in the study done by Drechsler et al. [22]. Gender differences were also noted in serum sclerostin, being significantly higher in male gender in both non-dialyzed cases as well as total number of CKD cases. Such a finding was in agreement with the results of Kanbay et al. [18] and Asamiya et al. [23] whom reported a significant increase in serum sclerostin levels in males compared to females.

Significant positive relations of serum sclerostin with age as well as with valvular calcification were demonstrated in our study in both groups of CKD patients. Brandenburg et al. [24] found that there was an increased expression of sclerostin in calcified aortic valves than in non-calcified valves and concluded that sclerostin is locally produced in aortic valve tissue adjacent to areas of calcification. Moreover, Koos et al. [25] found a significant correlation between serum sclerostin level and valvular calcification. The present study failed to demonstrate a significant correlation between serum sclerostin and CIMT or carotid plaque calcification in both groups of patients. This was in agreement with results of Thambiah et al. [26] whom demonstrated the lack of a significant correlation between serum sclerostin and a surrogate marker of arterial stiffness which was contour analysis of digital volume pulse in CKD patients. Wang et al. [27] demonstrated a significant association between serum sclerostin and abdominal aortic calcification with higher values being predictive of reduced short-term CV events in CKD cases stages 3-5D. Kirkpantur et al. [28] demonstrated in their study an independent association between serum sclerostin and CIMT, with serum sclerostin being higher in patients with carotid plaques compared to patients without plaques denoting an up-regulated sclerostin expression in osteogenically transformed VSMCs. It is worth mentioning that the study of kirkpantur et al. [28] was conducted on diabetic patients where diabetes increases the risk of VC which was not the case in our study, with diabetic patients being excluded. Furthermore, the lack of association in our study may be attributed to a lower percentage of patients presenting with calcified carotid plaques (17.5%) compared to patients without calcified plaques (82.5%). The inconsistent results concerning the correlation between serum sclerostin and VC can be attributed to the relatively small sample size, heterogeneity in enrolled cases, and discrepancy in anatomical structure examined.

Our study identified a significant inverse relation of serum sclerostin with eGFR in all CKD cases. This was in agreement with the results of Morena et al. [29] who demonstrated an increase in serum sclerostin with declining renal function, anticipating a potential role for renal clearance in contributing to serum sclerostin level. Despite the lack of a statistically significant correlation between serum sclerostin level and total body fat or lipid profile among the three groups in this study, yet Wnt signaling pathway along with its natural inhibitor sclerostin protein are implicated in regulating adipogenesis, body fat distribution, and susceptibility to obesity[9].

In this study, the best cutoff values obtained for serum sclerostin as a potential biomarker for both types of calcification revealed that sclerostin was more of a sensitive rather than a specific biomarker. Bruzzese et al. [30] reported serum sclerostin as a reliable biomarker of VC based on a ROC curve generated cutoff value of 1.15 ng/mL (50.6 pmol/L). As regard valvular calcification, the present study to the best of our knowledge was the first to use ROC curve modality in addressing the sensitivity and the specificity of serum sclerostin as a potential biomarker of valvular calcification.

The multiple linear regression analysis done revealed that valvular calcification, eGFR, and male gender were independent predictors of serum sclerostin level (Table 4). Brandenburg et al. [24] showed through multiple regression analysis an independent association between serum sclerostin and aortic valve calcification. The present study however failed to demonstrate an independent contribution of age, BMI, and carotid calcification to serum sclerostin level, where old age and morbid obesity were excluded from our study, along with the lower

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**Table 4. Multiple linear regression analysis for factors that can contribute to serum sclerostin level.**

| Model                      | Regression Coefficients | t-Test | p-Value | 95% Confidence Interval for B | Lower Bound | Upper Bound |
|----------------------------|-------------------------|--------|---------|-------------------------------|------------|-------------|
| (Constant)                 | β: Regression Coefficients; SE: standard error. |        |         |                               |            |             |
| Gender                     | 47.253                  | 20.943 | 2.256   | 0.027                         | 5.533      | 88.973      |
| Valvular calcification     | 9.949                   | 4.729  | 2.104   | 0.039*                        | 0.528      | 19.371      |
| Estimated GFR              | 23.745                  | 4.527  | 5.246   | 0.000*                        | 14.727     | 32.762      |
|                            | −12.167                 | 3.530  | −3.446  | 0.001*                        | −19.199    | −5.134      |

β: Regression Coefficients; SE: standard error.
percentage of cases (17.5%) experiencing carotid calcification.

Some limitations need to be addressed in this study. First; the relatively small number of non-obese diabetes free patients included in this study. Second; all CKD cases experiencing carotid plaque calcification, whether non-dialyzed or dialyzed, were fewer in number (17.5%) compared to cases not experiencing plaque calcification (82.5%).

6. Conclusion

In conclusion, our work identified serum sclerostin as a potential sensitive rather than a specific biomarker of both vascular and valvular types of calcification across all CKD cases, with male gender, valvular calcification, and eGFR acting as independent contributors to its serum level. The sclerostin expressed in calcified valves and plaques may undermine the mineralizing power of ALP in osteo/chondrogenically differentiated VSMCs. Addressing the therapeutic potential of sclerostin in attenuating the calcification process that develops in CKD has gained some attention [11], and could represent a point of future research.

Disclosure statement

No potential conflict of interest was reported by the authors.

Notes on contributors

Moyassar Ahmad Zaki has an MD Degree in Chemical Pathology and is Professor of Chemical Pathology at the Medical Research Institute, Alexandria University.

Thanaa Fathi Moghazy has an MD Degree in Chemical Pathology and is Professor of Chemical Pathology at the Medical Research Institute, Alexandria University.

Noha Said Kandil has an MD Degree in Chemical Pathology and is Lecturer of Chemical Pathology at the Medical Research Institute, Alexandria University.

Dalia Aly Maharem has an MD Degree in Nephrology and is Assistant Professor of Internal Medicine at the Medical Research Institute, Alexandria University.

Khaled Aly Matrawy has an MD Degree in Radiodiagnosis and is Assistant Professor of Radiodiagnosis at the Medical Research Institute, Alexandria University.

Alaa Mohamed Ismail El-Banna has an MSc in Chemical Pathology and is at the Medical Research Institute, Alexandria University.

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