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Correlation of Serum Vitamin D Levels to Vascular Access Dysfunction in Prevalent Hemodialysis

Mona Hosny Abdel Salam[1], Reem Jan Farid[2], Mostafa Abdelnassier Abdelgawad[1] and Marwa Salim Youssef Ismail[3]

[1]Internal Medicine Department, Faculty of Medicine, Ain Shams University, Egypt.
[2] Clinical Pathology Department, Faculty of Medicine, Cairo University, Egypt.
[3]Central Hospital of Bassioun / Gharbea Governorate, Ministry of Health Egypt.
salamhosnymona2015@gmail.com; drmona_abdelsalam@med.asu.edu.eg

Abstract: Vascular access dysfunction in hemodialysis patients has been correlated to low serum vitamin D level in previous studies. Vitamin D deficiency and hepatitis C virus infection have been linked to endothelial cell dysfunction, promoting inflammatory cascade.30 negative - & 30 positive - hepatitis C virus patients on prevalent hemodialysis in Ain Shams University Hospitals, were enrolled in the study. All patients had access blood flow < 800 ml / min. For all patients we performed: complete physical examination, complete blood count, serum ferritin, ESR 1st and 2nd hours, CRP, blood urea, serum creatinine, serum albumin, total and direct bilirubin, alanine transferase, aspartate transferase, prothrombin time, International Normalized Ratio, serum calcium and phosphorus, and serum intact parathyroid hormone. Previous laboratory tests were performed using conventional methods within our hospitals laboratories. Serum vitamin Dlevel was measured by Enzyme Linked Immunosorbent Assay. Access blood flow was measured by Duplex Ultrasound. Vitamin D serum level was < 20 ng/ml within negative and positive groups with no significant difference between them. Vascular access flow was significantly lower within positive patients. Parathyroid hormone, Phosphorus, Prothrombin time, International Normalized Ratio, Alanine - and Aspartate - transferase were significantly higher within positive patients. We deduced that Vitamin D level < 20ng /ml was associated with reduced vascular access blood flow < 800 ml / min, with much more reduced access flow within hepatitis C virus positive patients.

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Key Words: Hemodialysis – vitamin D – HCV – Vascular access blood flow.

1. Introduction

An adequate vascular access blood flow is mandatory for an efficient hemodialysis procedure[1].

Studies have reported that vascular dysfunction state in patients on regular hemodialysis was responsible for 20 % of total hospital admissions within those patients[2].

Beside its effects on mineral metabolism, vitamin D has got receptors within many tissues in human body including brain, cardiomyocytes, vascular smooth muscle cells, endothelial cells, and others [3]. Vitamin D has got many pleeotropic effects including among which protection against oxidative stress, anti – inflammatory, and immune modulating effects[4]. It inhibits endothelial dysfunction, promotes endothelial cell healing through endothelial growth factor secretion stimulation, and finally this inhibits vascular smooth cells migration and proliferation, and hence decreasing vascular access caliber and flow[5].

Vitamin D deficiency results in a disordered response of adaptive immunity, allowing inflammatory processes to take place, eventually leading to vascular dysfunction [3, 6].

A strong relationship has been reported between vitamin D level having receptors within vascular walls, and both the degree of vascular walls abnormalities and markers of atherosclerosis, including highly sensitive CRP [7].

2. Patients and Methods

This is an observational case control study. Sixty patients on prevalent hemodialysis from Ain Shams University Hospitals hemodialysis units, were included in the study. Patients age ranged from 18 to 50 years. An informed consent was obtained from all patients. Patients included in our study suffered from increased intima – media thickness and decreased pulse wave velocity in arteriovenous fistula, and had an estimated arteriovenous fistula blood flow ≤ 800 ml / min by Duplex ultrasound denoting access dysfunction, as reported by Hosny Abdel – Salam et al.[8].

Thirty patients were hepatitis C virus positive (+ve group) and the remaining thirty were hepatitis C virus negative (-ve group).

Patients having malabsorption, a BMI > 35, athrombosed fistula at the time of the study, on medications that decrease vitamin D level in blood or a disease that increase vitamin D level in blood, Diabetes Mellitus and liver cirrhosis with liver cell failure (Child Pough C), on medication decreasing vitamin D level or having a disease increasing its level were excluded from the study.

2. Methods

Complete physical examination was performed for all patients. Body mass index (BMI) was calculated in kg/ m^2 (BMI> 25 is considered as overweight). For all patients the following laboratory tests were done according to conventional methods used in Ain Shams University Hospitals laboratories, (normal ranges for our laboratories were mentioned beside each test):

Complete blood count including: Hemoglobin [in males (15.7 ± 4 gm /dl) and in females (13.8 ± 1.5 gm / dl)], TLC [4.3 – 10.3 (X 10^3 / µL)], platelets [150 – 300 (x 10^{-6} cells / L)], Ferritin (in males 12 – 300 ng / ml and in females 12 - 150 ng / ml), ESR (in males 1st hour 3 – 5 mm & 2nd hour 6 – 10 mm, and in females 1st hour 8 – 10 mm & 2nd hour 16 – 20 mm), CRP (< 6 = negative), serum urea (5 – 20 mg / dl), serum creatinine (0.4 – 1.5 mg / dl), serum albumin (3.5 - 5.5 gm / dl), total bilirubin (0.1 – 0.2 mg / dl), direct bilirubin (0.0 – 0.4 mg / dl), serum alanine transferase (ALT = 7 – 55 Units / L), serum aspartate transferase (AST = 10 – 40 Units /L), serum albumin (3.5 – 5.5 g / dl), Prothrombin time (PT = 11 – 13.5 seconds), International Normalized Ratio (INR = 0.8 - 1.1), serum calcium (Ca = 8.5 - 10 mg / dl), serum phosphorus (P = 2.4 - 4.5 mg / dl), and serum intact Parathyroid hormone (PTH = 10 - 65 pg / ml).

Measurement of serum vitamin D: by ELISA based on the concept that antibodies detecting 25 – OH vitamin D 2 and 25 – OH vitamin D 3 are bound onto microwells. We used ORGENTEC Diagnostika GmbH, Carl - Zeiss - Straβe 49 – 51 55129 Mainz - Germany. (www. Orgentec.com). E – mail: Orgentec@orgentic.com [9].

Reference range for 25 – OH vitamin D3 / D2 [10]: sufficient level of vitamin is considered to be > 30 ng/ml, values of 21 – 29 ng / ml are considered to be insufficient, and values < 20 ng / ml indicate severe deficiency.

Duplex Ultrasound

Duplex ultrasound was performed to detect patency, increased media thickness, reduced pulse wave velocity, and subsequent flow rate within hemodialysis arteriovenous fistula. The device used was manufactured on 12 December 2013, for Philips Ultrasound, Bothell, Washington USA 98021. Model: HD7. Volt: 100 – 240 V. FREQ: 50/60 Hz. Input Power 780 VA. CLASS: I. Part number: 989605368681. Manufactured by Philips and Neusoft Medical Systems Co., Ltd. Address: Neusoft Park, Hun Nan Industrial Area, Shenyang 110179, China.

Table 1: Comparison of HCV negative group (HCV - VE gp) and HCV positive group (HCV + VE gp) as regards age, weight, height, BMI, systolic blood pressure, and diastolic blood pressure:

	HCV -ve gp (mean± SD	HCV + GP (mean ± SD)	t –test P value
Age	43.9 ± 7.86	42.03 ± 8.29	0.37
Weigh	67.37 ± 11.61	66.87 ± 13.16	0.87
Height	1.67 ± 0.12	1.7 ± 0.14	0.31
BMI	24.79 ± 4.71	23.63 ± 5.32	0.37
Systolic blood pressure	127.67 ± 26.22	127 ± 23.0	0.91
Diastolic blood pressure	78 ± 13.49	77 ± 13.17	0.77

Data management and analysis

Collected data was revised, coded, tabulated, and introduced to a PC using Statistical Package for Social Science (SPSS 20).

1. Descriptive statistics: Mean, Standard Deviation (±) and range for parametric numerical data, while Median and Interquartile range (IQR) for non - parametric numerical data. Frequency and percentage were performed for non - numerical data.

2 - Analytical statistics comprised Student T test to assess the statistical significance of the difference between two study group means, Mann Whitney Test (U test) to assess the statistical significance of the difference of non – parametric variables between the two studied groups, and Chi – Square test to examine the relationship between two qualitative variables. P value < 0.05 is considered significant, P < 0.01 is highly significant, and P > 0.05 is non – significant. Correlation analysis (using Pearson s method) was

performed to assess the strength of association between two quantitative variables. The correlation coefficient (Pearson" s and Spearman " s denoted symbolically " r " and " rs " respectively) defines the strength (magnitude) and direction (positive or negative) of the linear relationship between two variables. r value of 0 – 0.19 is regarded as very weak correlation, r = 0.2 -0.39 as weak correlation, r =0.40 – 0.59 as moderate correlation, r = 0.6 – 0.79 as strong correlation, and r = 0.8 - 1 as very strong correlation. Linear regression analysis was used to test and estimate the dependence of a quantitative variable based on its relationship to one or more independent variables.

3. Results

Table 2: Comparison of HCV -VE group and HCV +VE group as regards vitamin D level, vascular access blood flow (access bl. Fl.), parathyroid hormone (PTH), calcium, phosphorus, hemoglobin (H b), total leucocyte count (TLC), and platelet count (PLT).

	HCV –VE gp	HCV+VE gp	t – test
	Mean ± SD Median (IQR)	Mean ± SD Median (IQR)	P value
Vitamin D	11.48 ± 5.42	10.07 ± 6.27	0.35
Access bl. Fl	345 (240 – 550)	190 (120 – 350)	0.03[M]
PTH	200.45(102 – 376)	536.5 (246 – 800)	0.002[M]
Calcium	8.78 ± 0.96	8.41 ± 1.2	0.2
Phosphorus	4.12 ± 1.64	5.07 ± 1.63	0.02
Hb	9.92 ± 2.09	9.26 ± 1.79	0.19
TLC	6.2 ± 2.13	9.78 ±16.88	0.05
PLT	237.9 ± 87.93	204.5 ± 79.52	0.12

[M]= Man Whitney test

Table 3: Comparison of HCV – VE group and HCV +VE group as regards serum ferritin, serum albumin, total bilirubin (T. Bil.), direct bilirubin (D. Bil.), PT, INR, ALT, and AST.

	HCV –VE gp	HCV+VE gp	t – test
	Mean ± SD Median (IQR)	Mean ± SD Median (IQR)	P value
Ferritin	252 (159.4 – 694)	263.5 (179 – 527)	0.87[M]
Albumin	3.82 ± 0.57	3.55 ± 0.74	0.12
T. Bilirubin	0.88 ± 0.33	1.09 ± 0.68	0.14
D. Bilirubin	0.3 (0.2 – 0.6)	0.35 (0.1 – 0.9)	0.38[M]
PT	13.1 ± 1.01	14.79 ± 1.79	< 0.001
INR	1.91 ± 0.15	1.34 ± 0.31	0.02
ALT	23.45 ± 10.21	32.33 ± 14.61	0.009
AST	25.94 ± 10.65	32.8 ± 15.41	0.05

[M] = Mann Whitney test

Table 4: Comparison of HCV -VE group and HCV +VE group as regards serum urea, serum creatinine, ESR 1st hour, ESR 2nd hour, and CRP.

	HCV –VE gp	HCV+VE gp	t – test
	Mean ± SD Median (IQR)	Mean ± SD Median (IQR)	P value
Urea	115.43 ± 52.51	116.45 ± 33.2	0.92
Creatinine	7.65 (6.1 – 12.5)	7.55 (6.9 – 8.9)	0.64[M]
ESR 1st hour	35.6 ± 25.33	31.57 ± 21.41	0.50
ESR 2nd hour	52.27 ± 28.88	51.43 ± 25.67	0.90
CRP	7.83 ± 2.78	7.6 ± 3.83	0.78

[M] = Mann Whitney test

4. Discussion

It seems that in normal health state human needs a minimum circulating blood level of 20 ng / ml of 25 (OH) D for the kidney to be able to generate 1.25 (OH) 2 D necessary for calcium and phosphorus mineral metabolism maintenance. But human body needs a higher blood level of 25 (OH) D for maintaining cellular functions at maximal health because at this level, extrarenal tissues contribute to converting 25 (OH) D to 1,25 (OH) 2 D [11].

Vitamin D deficiency (<20 ng/L) or insufficiency (20 -29 ng /L) are common among patients with chronic kidney disease (CKD) or undergoing dialysis [12].

In our study, low access flow volume was associated with low Vitamin D serum level (< 20 ng/ml) within both negative and positive groups, in agreement with Agarwal et al. [13], without significant difference between the two groups (table 2). Abnormally low value of vitamin D was associated with poor vascular access outcome [14]. Vitamin D didn't show any significant correlation to access flow volume (rs = 0.027, P = 0.88) within negative group and a weak correlation within the positive group (rs = - 0.322, P value = 0.08) within the positive group using Spearman correlation test. This finding was confirmed by a linear regression analysis (Regression Coefficient=- 5.566, 95 % CI = -15.62 - 4.49, P = 0.27). This suggested that in case of having access flow < 600 ml / min with vitamin D < 20 ng / ml in hemodialysis patients, vitamin D level and access flow volume inter –relationship could not be proved statistically whether HCV infections was present or not.

Vascular access estimated blood flow mean value was below minimal level of 800 ml/min[8], and even below 600 ml /min[15], within both negative and positive groups. Access flow volume was significantly higher within negative group (nearly twice mean value) as compared to positive group, (table 2). We could not confirm a direct impact of HCV infection upon access flow volume according to a linear regression analysis (Regression Coefficient = -40.679, 95 % CI = - 176.01 – 94.66, P = 0.55). This could be explained as an indirect effect of HCV on vascular access function through cryoglobulinemia - induced vasculitis, which was suggested by a significantly higher TLC within positive patients as reported by Daniel et al.[16]. The principal lesion within this vasculitis was found to be endothelial cell injury accompanied by necrosis of small caliber vessels, and inflammatory response settlement within these vessel walls infiltrated by lymphocytes, neutrophils, & cryoglobulins ending in a fibrin rich thrombus formation [17].

Systolic blood pressure was higher than normal within both groups without significant difference between them (table 1), which could mean a higher mechanical stress upon vascular access vessel walls, as reported by Tonelli et al [18]. We found a weak correlation of systolic blood pressure to serum vitamin D level within both negative (r = 0.251, P = 0.08) and positive patients (r = 0.282, P = 0.13) using pearson correlation test, and to vascular access flow volume within negative (rs = 0.093, P = 0.62) or positive (rs = 0.282, P = 0.13) using spearman correlation test.

PTH serum median level was higher than normal limit within both groups, partially due to vitamin D deficiency. PTH level was more than twice significantly higher within the positive group as compared to the negative group (table 2), and this could be due to a less PTH hormone clearance by a less efficient dialysis quality due to a reduced access flow volume within positive patients. PTH did not show any valid correlation with each of vitamin D level within negative patients (r =0.335, P = 0.071) or positive patients (r =-0.124, P =0.51) using Pearson correlation test, and access flow volume within negative patients (rs = 0.204, P = 0.28) or positive patients (rs =-0.259, P = 0.16) using Spearman correlation test.

Serum Calcium mean level was within the accepted range within negative and positive patients and serum phosphorus mean value was much significantly higher within positive patients with much lower access flow volume (table 2), possibly due to inefficient removal of excess phosphorus. Serum phosphorus did not have any significant relationship either to vitamin D level (r = 0.082, P = 0.66) within negative patients & (r =- 0.025, P = 0.89) within positive patients, using Pearson Correlation test, OR to access flow volume (rs =- 0.167, P = 0.37) within negative patients & (rs = - 0.044, P = 0.81) within positive patients, using Spearman Correlation test.

Liver enzymes AST & ALT were significantly higher within the positive patients (table 3), having a range with upper limit exceeding normal values. This reflected a going on low grade inflammatory process within positive patients, superadded to the uremic chronic inflammatory state already existing within both groups. PT & INR were found to be significantly higher within positive patients (table 3). PT has shown to have an impact on access flow volume through a linear regression analysis, (Regression Coefficient = - 42.296, 95 % CI = - 82.89 - -1.71, P = 0,04). AST & ALT were having a range with upper limit exceeding normal values, as HCV had a direct cytopathic effect on endothelial cells causing its injury which was observed in sinusoids of human liver [19]. But indeed inflammation markers were non – significantly lower

within positive group as regards ESR 1st hour, ESR 2nd hour, & CRP (table 4), which could mean that within positive patients the presence of uremic state has limited the inflammatory impact of chronic HCV infection.

5. Conclusion

Patients having low vascular access flow volume had low serum vitamin D levels (< 20 ng /ml), whether HCV negative or positive. The HCV positive hemodialysis patients had much lower vascular access flow, much higher PTH levels, serum phosphorus levels, PT, INR, AST and ALT than negative patients.

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Corresponding Author

Prof. Dr. Mona Hosny Abdel Salam
Professor of Internal Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt.
E-Mail: salamhosnymona2015@gmail.com; drmona_abdelsalam@med.asu.edu.eg

References

1. Collins AJ, Roberts TL, Peter WLS, Chen SC, Ebben J and Constantini E: United States renal data system assessment of the impact of the National Kidney Foundation- Dialysis Outcomes Quality Initiative guidelines. Am. J. Kidney Dis. (2002); 39 (4): 784 - 95.
2. Diskin C J, Stokes TJ, Dansby LM, Radcliff L and Carter TB: Understanding the pathophysiology of hemodialysis access problems as a prelude to developing innovative therapies. Nat. Clin. Pract. Nephrol. 2008; 4: 628 - 38.
3. Mheid I Al, Patel RS, Tangricha V and Quyyumi AA. Vitamin D and cardiovascular disease: Is the evidence solid?. European Heart Journal 2013; 34 (48): 3691 – 3698.
4. Chowdhury R, Kunutsor S, Vitezova A, Oliver – Williams C, Chodhury S, Kiefte – de – Jong JC, Khan H, Baena CP, Prabhakaran D, Moshe H, Feldman BS, Pan A, Johnson L, Crowe F, Hu FB and Franco OH. Vitamin D and risk of cause specific death: Systematic review and meta – analysis of observational cohort and randomized intervention studies. British Medical Jounal2014; 348, g 1903. Doi: 10.1136/bmj. g1903 (Published 1 April 2014).
5. Norman PE, and Powell TJ. Vitamin D and cardiovascular disease. Circulation research 2014; 114: 379.
6. Kempker JA, Tangpricha V, Zeigler T R and Martin G S. Vitamin D in sepsis; from basic science to clinical impact. Critical Care 2012; 16 (4): 316. (http://ccforum.com/content/16/4/316)
7. Van de Luijtgarden K M, Voute M T, Hoeks S E, Bakker EJ, Chonchol M, Stolker R J, Rowet EV and Verhagen H J M: Vitamin D deficiency may be an independent risk factor for arterial disease. European Journal of Vascular and Endovascular surgery 2012; 44(3): 301 -306.
8. Hosny Abdel - Salam M, El–Said T, Abdallah, A. Comparison of arteriovenous fistulae having blood flow equal to and higher than 800 ml /min as regards clinical and laboratory parameters. International Journal of Recent Scientific Research 2016;7 (10): 13499 - 13507.
9. Enko D, Kreigshauser G, Stolba R, Worf E, Halwachs – Baumann G. Method evaluation study of a new generation of vitamin D assays. Biomedica Media 2015; 25 (2): 203 – 12.
10. Holick M F. Vitamin D deficiency. New Engl. J. Medicine 2007; 357: 266 – 281.
11. Holick M F. Calcium and vitamin D. Diagnostics and therapeutics. Clin. Lab. Med. 2000; Sep. 20 (3): 569 – 90.
12. Jean G, Souberbielle J C, Chazot C. Vitamin D in chronic kidney disease and dialysis patients. Nutrients 2017; 9, 328. Doi:10.3390/nu9040328
13. Agarwal G, Vasquez K, Penagaluru N, Gelfond J, Qunibi WY. Treatment of vitamin D deficiency / insufficiency with ergocalciferol is associated with reduced vascular access dysfunction in chronic hemodialysis patients. Hemodialysis International 2015; 19 (4): 499 – 508.
14. Dusso AS. Update on the biologic role of the vitamin D on endocrine system. Curr. Vasc. Pharmacol. 2014; 12 (2): 272 – 277.
15. Ahmed Samy E, Abdelrahman AM, Elshafei M, Ashraf Adel O. and Sarah Ibrahim Ahmed. The relation between the level of serum Tumor Necrosis Factor - Alpha and hemodialysis adequacy in diabetic and non diabetic patients on maintenance hemodialysis. Urol. Nephrol. Open Access J. 2016; 3(2):00074, DOI: 10.15406/UNOAJ.2016,03,00074.
16. Daniel L, Fakhour F, Joly D, Mouthon L, Nusbaum P, Grunfeld JP, Schifferli J, Guillevin L, Lesavre P and Halbwachs – Mecarelli L. Increase of circulating neutrophil and platelet microparticles during acute vasculitis and hemodialysis. Kidney International 2006; 69: 1416 – 1423.

17. Barsoum RS, William EA, Khalil SS. Hepatitis C and kidney disease: a narrative review. Journal of Advanced Research 2017; 8: 113 – 130.
18. Tonelli M, Hirsch D, Chan CT, Marryatt J, Mossop P, Wile C and Jindal K. Factors associated with access blood flow in native vessel arteriovenous fistulae. Nephrology Dialysis Transplantation 2004, 19 (10): 2559 – 2563.
19. Barsoum RS. Hepatitis C virus: from entry to renal injury - facts and potentials. Nephrol Dialysis Transplantation 2007; 22 (7): 1840 – 8 J.

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