

VITAMIN D DEFICIENCY IN PATIENTS WITH ESSENTIAL HYPERTENSION

¹Akber Yousfani, ²Tariq Zaffar Shaikh, ³Majid Ali Soomro, ⁴Athar Hussain Memon, ⁵Jamrose Durrani, ⁶Zaheer Ahmed, ⁷Zulfiqar Ali Qutrio Baloch and ⁸*Syed Zulfiqar Ali Shah

¹MD, MCPS Assistant Professor Department of Medicine Unit-III Liaquat University Hospital Hyderabad / LUMHS, Jamshoro, Sindh Pakistan.

²MD Senior Registrar Department of Medicine Unit-I Liaquat University Hospital Hyderabad / LUMHS, Jamshoro, Sindh Pakistan.

³MD Assistant Professor Department of Medicine Unit-I Liaquat University Hospital Hyderabad / LUMHS, Jamshoro, Sindh Pakistan.

⁴House Officer Lyari General Hospital Karachi.

⁵Department of Medicine Liaquat University Hospital Hyderabad.

⁶General Practitioner Medeor 24 X7 Hospital, Abu Dhabi.

⁷Brandon Regional Hospital, Brandon, Florida.

⁸*Department of Medicine Liaquat University Hospital Hyderabad, Sindh, Pakistan.

*Corresponding Author: Dr. Syed Zulfiqar Ali Shah

Department of Medicine Liaquat University Hospital Hyderabad, Sindh, Pakistan.

Article Received on 16/09/2016

Article Revised on 06/10/2016

Article Accepted on 26/10/2016

ABSTRACT

Objective: To determine the frequency of vitamin D deficiency in patients with essential hypertension. **Patients and Methods:** This cross sectional descriptive study was conducted in department of Medicine and Cardiology at Liaquat University Hospital Hyderabad, Sindh, Pakistan. The inclusion criteria of the study were hypertensive patients for ≥ 03 months duration regardless of treatment, of 20-60 years of age and either gender presented at Liaquat University Hospital Hyderabad. All the subjects with essential hypertension will be further evaluate for the serum vitamin D level by taking 2 ml venous blood sample in a sterilize disposable syringe and sent to laboratory for analysis. Vitamin D deficiencies were defined as mild, moderate and severe respectively. All the data was analyzed in SPSS version 17, the frequency and percentages (%) was calculated for categorical variables while the mean \pm SD for quantitative variables. The Chi-square test was applied on categorical variables and P-value ≤ 0.05 was the level of significance. **Results:** During six months study period total 188 patients with essential hypertension were evaluated for vitamin D deficiency. The mean age \pm SD for overall population was observed as 44.76 ± 8.52 while it was 42.73 ± 7.55 and 49.98 ± 8.94 in male and female population respectively. The mean \pm SD of Vitamin D in vitamin D deficient essential hypertensive male and female population was 15.76 ± 3.72 and 8.97 ± 2.85 whereas the mean \pm SD of vitamin D in non deficient vitamin D essential hypertensive male and female population was 66.76 ± 4.74 and 54.99 ± 5.52 respectively. The vitamin D deficiency was observed in 109 (58%) patients $p < 0.01$ with male predominance (58.7%), $p = 0.03$. Of 109, 22 had mild, 44 had moderate and 43 had severe vitamin D deficiency. **Conclusion:** Overall the vitamin D levels are significantly low in relation to age, gender and severity in patients with essential hypertension.

KEYWORDS: Hypertension, Vitamin D and dihydroxycholecalciferol.

INTRODUCTION

Vitamin D derived from endogenous ultraviolet rays and formed in the skin, the high rate for vitamin D deficiency can be due to lifestyle related decrease in exposure to sun light.^[1] Vitamin D responsible for mineral and bone metabolism but has also suggests a role in extra-skeletal disorders.^[2] Formerly it was observed that vitamin D associated with lower plasma renin activity in hypertensive individuals.^[3] However, Tomaschitz, et al reported that vitamin D was inversely associated with plasma renin and angiotensin II concentrations in subjects referred for coronary intervention.^[4]

Cardiovascular disorders are variably associated with vitamin D and the literature linked blood pressure, vitamin D and related hormones since decades.^[5] Essential hypertension (EH) is due to disturbance between vasoconstriction and vasodilation and more in favor of vasoconstriction regulated by genetic and epigenetic factors. When the balance is disturbed leads to trigger vasoconstriction shift by vitamin D deficiency as an epigenetic factor.^[6] It has been observed that activated vitamin D (1,25-dihydroxyvitamin D [1,25(OH)2D]) blocks renin expression in the juxtaglomerular apparatus and blocks the proliferation of the vascular smooth

muscle cells responsible for blood pressure influence.^[7] Vitamin D (antiricketic factor) also called as sunshine vitamin because sunlight exposure is the best source compared to dietary source as by other vitamins.^[8] There has been shortage of literature regarding the vitamin D deficiency as a risk factor for a variety of diseases.^[9] The role of vitamin D deficiency in different disorders has not been well studied in Pakistan although hypovitaminosis D was detected to be a risk factor for development of hypertension in western population but there are no studies in such regard conducted in the Pakistani population. Therefore by considering such need in mind the present study was conducted in the department of cardiology at tertiary care teaching governmental hospital for evaluating the vitamin D deficiency in patients with essential hypertension so that proper and preventive measures can be taken according to the findings of the study and the results were also shared to create effective strategy as far as medical work up and management of essential hypertension is concerned.

PATIENTS AND METHODS

This cross sectional descriptive study was conducted in the department of cardiology at Liaquat University Hospital Hyderabad. The essential hypertension was labeled when the average of two or more diastolic blood pressure measurements on at least two subsequent visits is ≥ 90 mmHg or when the average of systolic blood pressure multiple readings on ≥ 02 subsequent visits was ≥ 140 mm Hg. The inclusion criteria of the study were hypertensive patients for ≥ 03 months duration regardless of treatment, of 20-60 years of age and either gender presented at Liaquat University Hospital Hyderabad while the exclusion criteria were non cooperative patients who refused to give consent or participate in the study, known / diagnosed cases for blood disorders (myeloproliferative disease, leukaemia lymphomas), chronic lung, liver and kidney disease, Cushing / Conn's syndrome, hyper/hypo parathyroidism, acromegaly,

obstructive sleep apnea, hyperthyroidism, polycystic kidney disease, coarctation of the aorta, renal artery stenosis and pheochromocytoma, connective tissue / autoimmune disorders, infectious and inflammatory disorders, the patients have history and evidence of using steroids, immunosuppressive, chemotherapeutic or already on antiarrhythmic drugs (lithium and amiodarone), anti-inflammatory or antibiotics therapy and pregnant ladies diagnosed as pre-eclampsia, HELLP syndrome and eclampsia. All the subjects with essential hypertension will be further evaluate for the serum vitamin D level by taking 2 ml venous blood sample in a sterilize disposable syringe and sent to laboratory for analysis. Vitamin D deficiencies were defined as mild (20-30 ng/mL), moderate (10-20 ng/mL) and severe (< 10 ng/mL) respectively. The informed consent was taken from every relevant individual and the data was collected on pre-designed proforma. All the data was analyzed in SPSS version 17, the frequency and percentages (%) was calculated for categorical variables while the mean \pm SD for quantitative variables. The Chi-square test was applied on categorical variables and P-value ≤ 0.05 was the level of significance.

RESULTS

During six months study period total 188 patients with essential hypertension were evaluated for vitamin D deficiency. The mean age \pm SD for overall population was observed as 44.76 ± 8.52 while it was 42.73 ± 7.55 and 49.98 ± 8.94 in male and female population respectively. The mean \pm SD of Vitamin D in vitamin D deficient essential hypertensive male and female population was 15.76 ± 3.72 and 8.97 ± 2.85 whereas the mean \pm SD of vitamin D in non deficient vitamin D essential hypertensive male and female population was 66.76 ± 4.74 and 54.99 ± 5.52 respectively. The demographical distribution and frequency and percentage for vitamin D in patients with essential hypertension in relation to age, gender and severity is shown in Table 01-04.

TABLE 01: THE DISTRIBUTION OF AGE AND GENDER

| | | GENDER | | Total | P-value |
|--------------|-------|--------|--------|--------|---------|
| | | Male | Female | | |
| AGE (yrs) | 20-29 | 15 | 13 | 28 | 0.006* |
| | | 12.3% | 19.7% | 14.9% | |
| | 30-39 | 39 | 12 | 51 | |
| | | 32.0% | 18.2% | 27.1% | |
| | 40-49 | 46 | 17 | 63 | |
| | | 37.7% | 25.8% | 33.5% | |
| | 50-60 | 22 | 24 | 46 | |
| | | 18.0% | 36.4% | 24.5% | |
| Total | | 122 | 66 | 188 | |
| | | 100.0% | 100.0% | 100.0% | |

*P-value statistically significant.

TABLE 02: VITAMIN D DEFICIENCY IN RELATION TO AGE

| | | VITAMIN D DEFICIENCY | | Total | P-value |
|--------------|-------|----------------------|--------|--------|---------|
| | | Yes | No | | |
| AGE (yrs) | 20-29 | 26 | 2 | 28 | <0.01* |
| | | 23.9% | 2.5% | 14.9% | |
| | 30-39 | 24 | 27 | 51 | |
| | | 22.0% | 34.2% | 27.1% | |
| | 40-49 | 37 | 26 | 63 | |
| | | 33.9% | 32.9% | 33.5% | |
| | 50-60 | 22 | 24 | 46 | |
| | | 20.2% | 30.4% | 24.5% | |
| Total | | 109 | 79 | 188 | |
| | | 100.0% | 100.0% | 100.0% | |

*P-value statistically significant.

TABLE 03: VITAMIN D DEFICIENCY IN RELATION TO GENDER

| | | VITAMIN D DEFICIENCY | | Total | P-value |
|--------|--------|----------------------|--------|--------|---------|
| | | Yes | No | | |
| GENDER | Male | 64 | 58 | 122 | 0.03* |
| | | 58.7% | 73.4% | 64.9% | |
| | Female | 45 | 21 | 66 | |
| | | 41.3% | 26.6% | 35.1% | |
| Total | | 109 | 79 | 188 | |
| | | 100.0% | 100.0% | 100.0% | |

*P-value statistically significant.

TABLE 04: SEVERITY OF VITAMIN D DEFICIENCY IN RELATION TO GENDER

| | | SEVERITY | | | Total | P-value |
|--------|--------|----------|----------|--------|--------|---------|
| | | Mild | Moderate | Severe | | |
| GENDER | Male | 12 | 32 | 20 | 64 | 0.04* |
| | | 54.5% | 72.7% | 46.5% | 58.7% | |
| | Female | 10 | 12 | 23 | 45 | |
| | | 45.5% | 27.3% | 53.5% | 41.3% | |
| Total | | 22 | 44 | 43 | 109 | |
| | | 100.0% | 100.0% | 100.0% | 100.0% | |

*P-value is statistically significant.

DISCUSSION

The study recruited limited number of individuals because of the health institutional setup of under developed country. Vitamin D levels were evaluated and categorized in mild, moderate and severe by various studies formerly.^[10] In present study only 42% had sufficient levels above 30 ng/ml and this finding is consistent with other studies conducted by Pilz S, et al.^[11] This is because of the fact that majority of Pakistani population gained significant amounts of exposure to sun light and also emphasized to more importance on the improvement of dietary intake. Levels of 25 (OH) D were significantly lower in hypertensive population (57.9%), the mean \pm SD of Vitamin D in vitamin D deficient essential hypertensive male and

female population was 15.76 ± 3.72 and 8.97 ± 2.85 whereas the mean \pm SD of vitamin D in non deficient vitamin D essential hypertensive male and female population was 66.76 ± 4.74 and 54.99 ± 5.52 respectively. The difference for vitamin D status in relation to age and gender was statistically significant. There are no Pakistani research studies in relation to vitamin D in hypertension or similar disorders. Although international literature is available in such context, which concluded that vitamin D supplementation is mandatory for the prevention or control of hypertension and higher dietary intake of vitamin D results in effective control of hypertension with proved statistical significance.^[12,13] Vitamin D analogs had proven role in renin angiotensin axis suppression experimentally. In present study,

vitamin D levels were studied in various age groups with statistical significance and it is consistent with the study by Velayudhan G, et al.^[14] The relation of dietary intake and sunlight exposure of vitamin D were not conclusive in present study but there is a recommendation that dietary intake is the best source for vitamin D.^[15] The matter here being to debate that vitamin D levels have not been standardized across the Pakistani foods, the dietary supplements was evaluated through questionnaire where bias is most likely.^[16] Exposure to sun light was also evaluated by questionnaire and cross checking was scarce. The final logical interpretations of significant association between BMI and physical activity, sun exposure and physical activity and dietary intake and physical activity are matters of logical inference. In present study the male population was predominant as vitamin D deficient essential hypertensive individuals and it is consistent with the study by Forman JP, et al.^[17] Regarding the severity, the moderate to severity categories were more frequently observed and were also detected formerly by Siadat ZD, et al.^[18]

CONCLUSION

Overall the vitamin D levels are significantly low in relation to age, gender and severity in patients with essential hypertension. Thus, proper dietary intake of vitamin D has a low risk for developing hypertension. Physical activity and sunlight exposure adequately are protective measure against essential hypertension.

REFERENCES

1. Bikle DD. Vitamin D metabolism, mechanism of action and clinical applications. *Chem Biol.* 2014 Mar 20; 21(3): 319-29.
2. Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Wetterslev J, Simonetti RG, et al. Vitamin D supplementation for prevention of mortality in adults. *Cochrane Database Syst Rev.* 2014 Jan 10; (1): CD007470.
3. Majumdar V, Prabhakar P, Kulkarni GB, Christopher R. Vitamin D status, hypertension and ischemic stroke: a clinical perspective. *J Hum Hypertens.* 2015; 29(11): 669-74.
4. Tomaschitz A, Pilz S, Ritz E, Grammer T, Drechsler C, Boehm BO, et al. Independent association between 1,25-dihydroxyvitamin D, 25-hydroxyvitamin D and the renin-angiotensin system: the Ludwigshafen Risk and Cardiovascular Health (LURIC) Study. *Clin Chim Acta.* 2010; 411: 1354-1360.
5. Zittermann A. Vitamin D and cardiovascular disease. *Anticancer Res.* 2014; 34(9): 4641-8.
6. Vimalaswaran KS, Cavadino A, Berry DJ; Life Lines Cohort Study investigators, Jorde R, Dieffenbach AK, et al. Association of vitamin D status with arterial blood pressure and hypertension risk: a mendelian randomisation study. *Lancet Diabetes Endocrinol.* 2014; 2(9): 719-29.
7. Tamez H, Thadhani RI. Vitamin D and hypertension: an update and review. *Curr Opin Nephrol Hypertens.* 2012 Sep; 21(5): 492-9.
8. Matyjaszek-Matuszek B, Lenart-Lipińska M2, Woźniakowska E. Clinical implications of vitamin D deficiency. *Prz Menopauzalny.* 2015 Jun; 14(2): 75-81.
9. Haines ST, Park SK. Vitamin D supplementation: what's known, what to do and what's needed. *Pharmacotherapy.* 2012; 32(4): 354-82.
10. Hovsepian S, Amini M, Aminorroaya A, Amini P, Iraj B. Prevalence of vitamin D deficiency among adult population of Isfahan City, Iran. *J Health Popul Nutr.* 2011; 29(2): 149-55.
11. Pilz S, Tomaschitz A. Role of vitamin D in arterial hypertension. *Expert Rev Cardiovasc Ther.* 2010 Nov; 8(11): 1599-608.
12. Chen S, Sun Y, Agrawal DK. Vitamin D deficiency and essential hypertension. *J Am Soc Hypertens.* 2015 Nov; 9(11): 885-901.
13. Vaidya A, Forman JP. Vitamin D and hypertension current evidence and future directions. *Hypertension.* 2010; 56: 774-779.
14. Velayudhan G, Sasidharan PK. Vitamin d status in hypertension. *AJRFANS.* 2014; 14: 28-30.
15. Spiro A, Buttriss JL. Vitamin D: An overview of vitamin D status and intake in Europe. *Nutr Bull.* 2014 Dec; 39(4): 322-350.
16. Riaz H, Finlayson AE, Bashir S, Hussain S, Mahmood S, Malik F, et al. Prevalence of Vitamin D deficiency in Pakistan and implications for the future. *Expert Rev Clin Pharmacol.* 2016; 9(2): 329-38.
17. Forman JP, Scott JB, Ng K, Drake BF, Suarez EG, Hayden DL, Bennett GG, et al. Effect of vitamin D supplementation on blood pressure in blacks. *Hypertension.* 2013 Apr; 61(4): 779-85.
18. Siadat ZD, Kiani K, Sadeghi M, Shariat AS, Farajzadegan Z, Kheirmand M. Association of vitamin D deficiency and coronary artery disease with cardiovascular risk factors. *J Res Med Sci.* 2012 Nov; 17(11): 1052-5.