PARATHYROID HORMONE AND MAGNESIUM LEVELS IN VITAMIN D DEFICIENT FEMALES

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ABSTRACT

Vitamin D deficiency is a major health problem worldwide. In healthy subjects, vitamin D deficiency causes an increase in serum parathyroid hormone (PDH) level in response to hypocalcemia that in turn effectively restores serum calcium and phosphorus levels. However, the response in adult female in vitamin D deficient population in particular has not been studied especially in our set up. The objectives of this study were to determine the levels of iPTH and magnesium in vitamin D deficient adult females, among a sector of population living in a suburban area of Lahore.

Materials and Methods: A total of 125 asymptomatic apparently healthy women (aged 20 – 60 years) were included in this study. Subjects were randomly selected from the Shalamar / Mughalpura area in Lahore. The research was started after taking permission from ethical committee of UHS.

Results: In a total of 125 subjects, 59 (47%) had deficient, 41 (33%) had insufficient and 25 (20%) had sufficient levels of vitamin D. The serum iPTH level in vitamin D deficient women was significantly higher and an inverse correlation existed between vitamin D and iPTH. Magnesium levels, on the other hand deteriorated only with severe deficiency of vitamin D. This study indicates that serum iPTH is a better marker of detection of low vitamin D states, as compared to serum calcium and phosphorus levels which remain normal. Furthermore, magnesium levels must be monitored in vitamin D deficiency because of its implications in bone metabolism, muscular and cardiac activity.

Key words: Vitamin D, intact Parathyroid hormone (iPTH), Magnesium, 25 OH Vit D.

INTRODUCTION

Vitamin D deficiency has become a major health problem worldwide. Hydroxylation of vitamin D in the kidney is regulated closely by parathyroid hormone (PTH), hypocalcaemia, hypophosphataemia and is inhibited by 1,25-dihydroxyvitamin D.[1] Vitamin D deficiency is due to inadequate nutritional intake of vitamin D coupled with inadequate sunlight exposure, disorders that limit vitamin D absorption and conditions that impair the conversion of vitamin D into active metabolites including certain liver, kidney and hereditary disorders.[2,3] Vitamin D deficiency is significantly more common in women (83.9%) than in men (48.5%).[4-6]

Vitamin D deficiency can present as metabolic syndrome or osteomalacia.[7] PTH secretion occurs in response to hypocalcaemia, hypophosphataemia and calcitriol deficiency and is inhibited by severe hypomagnesaemia.[8] Like calcium (Ca), Magnesium (Mg) plays a role in the regulation of PTH secretion and it increases bone density. Mg is essential for the normal function of the parathyroid glands, metabolism of vitamin D and adequate sensitivity of target tissues to parathyroid hormone and active vitamin D metabolites. Mg is also necessary for vitamin D's beneficial actions on bones and supports calcium absorption by activating vitamin D into an active form that enables it to interact with calcium.[9,10] Haeney et al have shown that PTH can serve as a functional biomarker of vitamin D deficiency.[3] Deficiency in vitamin D causes high bone turnover, bone loss, mineralisation defects, hip and other fractures.[11,12] This study was designed to determine the levels and correlation of PTH and Magnesium in vitamin D deficiency in the more commonly affected gender – adult females.

METERIAL AND METHODS

A total of 125 asymptomatic apparently healthy women were included in this study. Subjects were randomly selected from the Shalamar / Mughalpura area in Lahore from middle socio-economic status. Written consent was taken from all the subjects for inclusion in the study. Inclusion criteria of this study were asymptomatic healthy women aged between 20 and 60 years while those having chronic renal failure or chronic diseases, chronic diarrhea, acute infection, pregnancy or those taking medication that can

modify bone metabolism were excluded.

Five ml blood was taken aseptically from each subject. Serum Mg was measured by colorimetric method. Serum iPTH was measured by immunochemiluminometric assay (ICMA) by using VITROS ECiQ Immuno-diagnostic Systems, using a kit from ortho clinic diagnostic UK. Serum 25-Hydroxy Vitamin D was measured by enzyme immunoassay, using a kit from immuno-diagnostic system. The data obtained were analysed using SPSS ANOVA test (tukey) was conducted among the three groups of 25OHD insufficiency. The association between serum 25OHD and iPTH concentration was studied by Pearson correlation. A *p*-value of less than 0.05 was considered statistically significant.

Table 1: *Values of demographic and biochemical parameters according to vitamin D levels.*

Parameters	*Group A (Mean ± SD) (n = 59)*	*Group B (Mean ± SD) (n = 41)*	*Group C (Mean ± SD) (n = 25)*	*P Value*
Age (years)	36.8 ± 12.0	38.9 ± 11.5	35.8 ± 10.5	0.520
BMI (kg/m)	24.1 ± 4.3	25.3 ± 3.6	23.2 ± 3.0	0.089
Vitamin D (nmol/l)	18.4 ± 5.2	48.84 ± 12.8[a]	93.5 ± 14.6[a,b]	0.001*
iPTH (pg/ml)	72.3 ± 31.8	53.0 ± 22.4[a]	40.38 ± 3.08[a,b]	0.001*
Magnesium (mg/dl)	1.86 ± 0.35	2.07 ± 0.19[a]	2.08 ± 0.19[a]	0.012*
Calcium (mg/dl)	9.09 ± 0.95	9.36 ± 0.60	9.58 ± 0.46[a]	0.025*
Phosphorus (mg/dl)	3.94 ± 0.60	3.99 ± 0.37	3.90 ± 0.70	0.821

*Statistically Significant Value ($p < 0.05$)
a = A vs B and A vs C (statistically significant)
b = B vs C (statistically significant)

RESULTS

The mean age of the subjects was 37.3 ± 11.6 years (range 20 – 60 years). The subjects were divided in three groups based on their serum vitamin D levels. Those with levels below 25 nmol/L were categorized to have deficient (Group A), levels between 25 – 75 nmol/L as insufficient (Group B) and levels more than 75 nmol/L as sufficient (group C). Out of 125 subjects, 59 (47%) had deficient, 41 (33%) had insufficient and 25 (20%) had sufficient levels of vitamin D. There was no significant difference among the three groups with regard to age and body mass index. Details of the parameters studied are given in Table 1.

DISCUSSION

In this study, we found low vitamin D levels (deficiency, insufficiency) in 80% of the subjects. A high prevalence of vitamin D deficiency has been found among all age groups in different populations reported in different studies.[15-17] Even apparently healthy individuals are prone to vitamin D deficiency. Various factors have been found to affect the prevalence of vitamin D deficiency. Probable factors for this deficient state may be indoor activity, decreased sun exposure, decreased body area exposed due to veiling and inadequate use of vitamin D supplementation (< 400 IU / day).

In the present study, analysis based on age subgroups showed minimum levels of vitamin D in women between 30 – 39 years of age. The women of this group fall mostly into the child bearing age and are largely confined to houses. Similar findings were noted in work done by Bagher (2004) where they demonstrated elderly female showed statistically significant higher serum levels of vitamin D compared with young and middle aged females.[18] Studies from Kashmir and other areas also showed a higher prevalence of vitamin D deficiency in females, which was most likely due to less sun exposure, less outdoor activities and decreased body area exposure compared to the male counterparts. Dietary norms may explain the high prevalence of this nutritional deficiency among our study subjects.[19-21] In our study, the biochemical data showed significantly increased levels of iPTH in subjects with low 25 – hydroxyvitamin D status. This findings is in accordance with similar previous studies.[22-26]

In this present study, we found a strong negative correlation between serum vitamin D and iPTH ($r = -0.422$, $p = 0.001$). This findings is in agreement with results reported by Zuberi (2008) demonstrating an inverse relationship between PTH and vitamin D levels.[27] The mean serum magnesium levels were low in the severe vitamin D deficient group but not in insufficient or sufficient groups which is in agreement with a previous study.[28]

The effectiveness and benefits of calcium with respect to bone health are impaired in the absence of adequate levels of magnesium in the body. It is difficult to get enough magnesium through diet because magnesium is eliminated from most processed foods. So magnesium has to be paired up with calcium and vitamin D in supplements.[29] The mean serum calcium levels were within normal limits in all three groups of our study subjects and showed no correlation between serum calcium and vitamin D levels as

reported by other studies.[25,27]

It is ***concluded*** that in this study, 80% of women showed vitamin D deficiency most likely of dietary origin. This study demonstrates that serum iPTH level in vitamin D deficient / insufficient individuals was significantly on higher side and inverse correlation exists between vitamin D and iPTH. This indicates that iPTH is a better biochemical marker of 25 – OH vitamin D deficiency, compared to the usual biochemical parameters serum magnesium, calcium and phosphorus, in the initial stages of declining 25 – hydroxyvitamin D levels in healthy population.

RECOMMENDATIONS

There is an urgent need for public education and awareness among medical professionals about the role of vitamin D in health in order to avoid the complications of vitamin D insufficiency and deficiency. Optimum sunlight exposure and lifestyle modifications can help to prevent the serum 25 – OH Vitamin D deficiency state. Vitamin D supplementation and vitamin D food fortification programs need to be implemented to avoid subsequent complications of this preventable condition. Furthermore, with 80% studied women falling below previously accepted normal range, a new reference range for Vitamin D needs to be ascertained, which is applicable to our population in our own set up.

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REFERENCES

1. Lips P, Hosking D, Lippuner K, et al. The prevalence of vitamin D inadequacy amongst women with osteoporosis: an international epidemiological investigation. J Intern Med. 2006; 260: 245.
2. Drezner MK, Motil KJ, Misra MS. Vitamin D insufficiency and deficiency in adolescents. J Nutr. 2011; 130: 26-48.
3. Heaney RP, Dowell MS, Hale CA, Bendich A. Calcium absorption varies within the reference range for serum 25 – hydroxyvitamin D. J Am Coll Nutr. 2003; 22: 142-6.
4. Gannage – Yared MH, Chemali R, Yaacoub N, Halaby G. Hypovitaminosis D in a sunny country: relation to lifestyle and bone markers. J Bone Miner. 2000; 15: 1856-62.
5. Looker AC, Pfeiffer CM, Lacher DA, et al. Serum 25 – hydroxyvitamin D status of the US population. Am J Clin Nutr. 2008; 88: 1519-27.
6. Mishal AA. Effects of different dress styles on vitamin D levels in healthy young Jordanian women. Osteoporos Int. 2001; 12: 931-5.
7. Grant WB, Holick MF. Benefits and requirements of vitamin D for optimal health: a review. Altern Med Rev. 2005 Jun; 10 (2): 94-111.
8. Kumar R, Thompson JR. The regulation of parathyroid hormone secretion and synthesis. J Am Soc Nephrol. 2011; 22 (2): 216-24.
9. Song V, Manson JE, Buring JE, Liu S. Dietary magnesium intake in relation to plasma insulin levels and risk of type 2 diabetes in women. Diabetes. 2003; 27: 59-65.
10. Risco F and Traba ML. Bone specific binding sites for 1,25 $(OH)_2D_3$ in magnesium deficiency. J. Physiol. Biochem. 2004; 60 (3): 199-204.
11. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. Endocr Rev. 2001; 22: 477-501.
12. Chapuy MC, Preziosi P, Maamer M et al. Prevalence of vitamin D insufficiency in an adult normal population. Osteoporos Int. 2002; 7: 439-43.
13. Parikh N, Guardia G, Eskridge T, Phillips E, Divine G, Rao DS. Prevalence of vitamin D depletion among subjects seeking advice on osteoporosis: a five – year cross – sectional study with public health implications. Osteoporos Int. 2008; 19 (1): 13.
14. Simonelli. The role of vitamin D deficiency in osteoporosis and fractures. Minn Med. 2004; 88: 34-36.
15. Schwalfengerg GK, Genuis SJ et al. Vitamin D supplementation in a nursing home population. Mol Nutr Food Res. 2010; 54 (8): 12072-6.
16. Kuriacose R, Olive KE. Prevalence of vitamin D deficiency and insufficiency in northeast Tennessee. South Med J. 2008; 101 (9): 906-9.
17. Bandeira F, Caldas G, Freese E, Griz L, Faria M, Bandeira C. Relationship between serum vitamin D status and clinical manifestations of primary hyperparathyroidism. Endocr Pract. 2002; 8: 266-70.
18. Bagher L, Hashemipour S, H Abidi, E Javadi, M Sedaghat, M Pajouhi, A et al. Vitamin D deficiency and causative factors in the population of Tehran. BMC Public health. 2004; 4 (1): 38-42.
19. Zargar AH, Ahmad S, Masoodi SR, et al. Vitamin D status in apparently healthy adults in Kashmir Valley of Indian subcontinent. Postgrad Med J. 2007; 83: 713-6.
20. Goswami R, Kochupillai N, Gupta N, Goswami D, Singh N, Dudha A. Presence of 25 (OH) D deficiency in a rural North Indian village despite abundant sunshine. J Assoc Physicians India. 2008; 56: 755-7.
21. Alagol F, Shihadeh Y, Boztepe H, et al. Sunlight exposure and vitamin D in Turkish women. J Endocrinol Invest. 2000; 23: 173-7.
22. Gordon CM, DePeter KC, Feldman HA, Grace E, Emans SJ, Prevalence of vitamin D deficiency among healthy adolescents. Arch Pediatr Adolesc Med. 2004; 158 (6): 531-7.
23. Glerup H, Mikkelsen K, Poulsen L, et al. Commonly recommended daily intake of vitamin D is not sufficient if sunlight exposure is limited. J Intern Med. 2000; 247: 260-8.
24. Mansoor S, Habib A, Ghani F, Fatmi Z, Badruddin S et al. Prevalence and significance of vitamin D deficiency and insufficiency among apparently healthy adults. Clin Biochem. 2010; 43: 1431-1435.
25. Masud F. Vitamin D levels for optimum bone health.

Singapore Med J. 2007; 48: 207-12.
26. Hashemipour S, Larijani B, Adibi H, Sedaghat M, Pajouhi M. The status of biochemical parameters in varying degree of vitamin D deficiency. J Bone Miner Metab. 2006; 24: 213-218.
27. Zuberi LM, Habib A, Haque N, Jabbar A. Vitamin D deficiency in ambulatory patients. J Pak Med Assoc. 2008; 58: 482-4.
28. Moe, S. Disorders involving calcium, phosphorus and magnesium. Prim Care. 2008; 35 (2): 215-37.
29. Bolland MJ, Grey A, Gamble GD, Reid IR et al. Calcium and vitamin D supplements and health outcomes: a reanalysis of the Women's Health Initiative (WHI). Am J Clin Nutr. 2011; 94 (4): 1144-9.