ORIGINAL ARTICLE

Vitamin D Deficiency among Adult Patients with Primary Hypothyroidism: A Preliminary Study Done in Anuradhapura, Sri Lanka

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ABSTRACT

The association between vitamin D deficiency and hypothyroidism is scarcely studied. A community-based, cross-sectional preliminary study was conducted to determine the prevalence and associated factors for vitamin D deficiency among adult patients with primary hypothyroidism in Anuradhapura, Sri Lanka. The study utilised a questionnaire, anthropometry, and laboratory analysis. A total of 79 patients were contacted by phone to verify eligibility, and 59 were deemed eligible. Among them, 55 consented and attended the assigned blood collection centre. However, data from one participant was excluded as the eGFR was <60 ml/min/1.73m^2. Hence, data from 54 participants were included for the final analysis. Most of the study participants were females (83%), rural residents (76%), and had associated non-communicable disease(s) (81%). All participants except two had a <10% 10-year risk of a fatal or non-fatal cardiovascular event. The mean (SD) duration of primary hypothyroidism was 8.4 (8.1) years, ranging from 0.25 to 8.5 years. The mean (SD) dose of thyroxine was 82.9 (33.9) µg, ranging from 25 to 200 µg. The mean (SD) vitamin D level was 14.6 (5.0) ng/ml, ranging from 5.3 to 26.9 ng/ml. Vitamin D sufficiency (≥20 ng/ml), insufficiency (12 to <20 ng/ml), and deficiency (<12 ng/ml) were reported in 13% (6-24), 54% (41-66), and 33% (22-47) participants, respectively. A comparison of study variables between the vitamin D sufficiency/insufficiency group and the vitamin D deficiency group did not reveal any significant differences. The findings provide an important lead for future large-scale studies. Comparison of findings among patients with other chronic diseases and healthy volunteers is proposed.

Keywords: Hypothyroidism, thyroxine, vitamin D deficiency

International Journal of Human and Health Sciences Vol. 10 No. 03 July'26

DOI:https://doi.org/10.31344/ijhhs.v10i3.957

INTRODUCTION

Vitamin D strengthens living organisms, and its deficiency may increase the risk of chronic inflammatory diseases and reduce life expectancy.[1] Prior literature highlights the association between vitamin D deficiency and hypothyroidism.[2] Globally, 15.7% of the total population were reported to have vitamin D deficiency (<30 nmol/l),[3] and the prevalence of primary hypothyroidism is 1 to 2%.[4] While congenital hypothyroidism has been frequently researched in Sri Lanka, research on adult primary hypothyroidism is scarce. A Sri Lankan study in the Colombo urban area found that 58.8% had a vitamin D level of <50 nmol/l.[5] The prevalence of vitamin D deficiency (<50nmol/l) among patients with hypothyroidism in America was 25.6% compared to 20.6% among normal controls.[2] Meanwhile, the prevalence of vitamin D deficiency among patients with hypothyroidism was reported to be 58% (<50 nmol/l) and 72% (cut-off not mentioned) among patients in India,[6] and Pakistan.[7] However, there is scarcity of literature available on similar research among Sri Lankan population. Still, vitamin D deficiency and hypothyroidism are health concerns in Sri Lanka.[5,8,9] Hence, this preliminary study aims to determine the prevalence and associated factors for vitamin D deficiency among adult patients

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with primary hypothyroidism in Anuradhapura, Sri Lanka.

METHODS

A community-based, cross-sectional study was conducted among adult patients with primary hypothyroidism in Anuradhapura, Sri Lanka. For the main study, a sample size of 384 needed according to Cochran's formula ($n = [Z^2xP(1-P)]/d^2$). For a preliminary study, 10% to 15% of the minimum sample size for the main study was estimated, i.e. between 38 and 58. Around 15 to 20 suitable adult patients with primary hypothyroidism per month are expected to attend a fee-levying pharmacy in Anuradhapura. Therefore, a minimum of 45 to 60 patients were expected to be recruited over 3 months. A three-month duration was chosen because the same cohort of patients was likely to revisit the pharmacy after that time duration. Patients with primary hypothyroidism, aged ≥18 years, Sinhala Buddhist, permanent residents in Anuradhapura for 3 years or more, and having an eGFR of 60 ml/min/1.73m^2 or more were included in the study. Different ethnicities in Sri Lanka showed a difference in the prevalence of vitamin D deficiency.[5] Therefore, Sinhala Buddhists were selected to have an ethnically homogeneous group. Exclusion criteria were: acute illness, presently on a vitamin D supplement, history of immunosuppression (steroid treatment or chemotherapy), pregnancy, everyday betel chewing, everyday smoking, and heavy alcohol use.[10,11] Diagnosed adult patients with primary hypothyroidism on thyroxine treatment were recruited for the study according to their clinical history. The investigator contacted the patients via telephone to verify their eligibility before inviting them to the study. A total of 79 patients were contacted by phone to verify eligibility, and 59 were deemed eligible. Among them, 55 consented and attended the assigned blood collection centre. However, data from one participant was excluded as the eGFR was <60 ml/min/1.73m^2. Hence, data from 54 participants were included for the final analysis.

The questionnaire included sociodemographic factors and the Depression Anxiety Stress Scale-21 (DASS-21).[12] The consumption of vitamin D-rich food was reported as follows: never, rarely (1-2 times a month), occasionally (1-2 times a week), and regularly (3 or more times a week). The socio-demographic questions were administered by the investigator. The DASS-21 translated into the Sinhala language was self-administered.[13] The face validity of the sociodemographic questions was established and pre-tested in 3 volunteers. The Cronbach's alpha of questions representing depression, anxiety, and stress of DASS-21 indicated good internal consistency in the responses with 0.8, 0.7, and 0.9, respectively. Anthropometric measurements of weight, height, waist circumference, and hip circumference were measured using a standard digital bathroom scale (SECA robusta 813 CE), stadiometer (SECA 213 CE 0123) and measuring tape, respectively. Blood pressure was measured using a standard aneroid desk model sphygmomanometer (ACCOSON CE 0413) after a 5-minute rest in the seated position. The average of two blood pressure measurements within a minute interval was used for the analysis. Trained phlebotomists and medical laboratory technicians performed blood collection and analysis at the assigned blood collection centre. Blood sample was analysed for total thyroid function test (TSH, free T3, free T4), 25-hydroxy vitamin D, serum calcium, HbA1c, total cholesterol, and serum creatinine. The method used for the analysis of total thyroid function test (TSH, free T3, free T4), 25-hydroxy vitamin D, serum calcium, HbA1c, total cholesterol, and serum creatinine were electrochemiluminescence (ECL), enzyme-linked immunosorbent assay (ELISA), colorimetric assay, high-performance liquid chromatography (HPLC), enzymatic colorimetric assay, and enzymatic colorimetric assay, respectively. Quality control was done using Bio-Rad immunoassay plus control 1, 2, 3, Bio-Rad high and low control (vitamin D), Bio-Rad assay chemistry control 1 & 2, Bio-Rad lyphochek diabetes low and high control, Bio-Rad assay chemistry control 1 & 2, and Gernorm and Gerpath quality control, respectively. Data was expressed as means with standard deviation for continuous variables, and frequencies with percentages for categorical variables. Also, the World Health Organization/ International Society of Hypertension (WHO/ISH) risk prediction chart for South-East Asian Region B was used to predict the 10-year risk of a fatal or non-fatal cardiovascular event.[14] The prevalence of vitamin D deficiency was computed as a point estimate with 95% CI. Mann-Whitney U test was performed [vitamin D sufficiency/ insufficiency group (≥12 ng/ml) vs. vitamin D deficiency group (<12 ng/

ml)]. A p-value <0.05 was considered statistically significant. Binary logistic regression was performed to determine the significant association between variables of interest and the presence of vitamin D deficiency [adjusted odds ratios (alpha exp(b)) with 95% CI; p<0.05]. The following definitions were used for this study: vitamin D sufficiency, insufficiency and deficiency were defined as a 25(OH)D concentration of ≥20 ng/ml (≥50 nmol/l), 12 to <20 ng/ml (30 to <50 nmol/l), and <12 ng/ml (<30 nmol/l), respectively,[15] while primary hypothyroidism was defined by thyroid-stimulating hormone (TSH) concentrations above the reference range (most commonly used 0.4–4.0 mIU/l) and free thyroxine concentrations below the reference range (dependent on the type of assay used and the population studied).[16]

RESULTS

Table 1 shows that among 54 study participants, the majority was female (83%), rural residents (76%), non-head of household (80%), educated up to the general certificate of education (advanced level) or below (52%), non-working population (76%), currently married (91%), not living alone at the household (98%), having a monthly household income of >100,000 LKR (52%), and had an associated non-communicable disease(s) and were on long-term treatment (81%). Further, most never consumed alcohol (89%), never smoked (96%), and never chewed betel (100%). Less than 10% 10-year risk of a fatal or non-fatal cardiovascular event was found in 96%. Parental or sibling history of non-communicable diseases was observed in 91%. The participants' mean (SD) age was 54.9 (11.5) years, ranging from 25 to 74 years. Years of residence at Anuradhapura were 41.3 (19.9) years (4 to 72). Hours of sleep were 6.9 (1.0) hours (5 to 8.5). The duration of primary hypothyroidism was 8.4 (8.1) years (0.25 to 8.5). The dose of thyroxine was 82.9 (33.9) µg (25 to 200). The hours of exposure to direct sun per week were 1.9 (4.9) hours (0 to 20). Table 2 shows the logistic regression analysis for comparison between the vitamin D sufficiency/ insufficiency group and the vitamin D deficiency group. Figure 1 shows that the most of the participants consumed fish (52%), egg (48%), and dairy products (56%) regularly. However, a high majority of participants (94%) have not consumed vitamin D-fortified food.

Vitamin D sufficiency (≥50 nmol/l), insufficiency (30 to <50 nmol/l), and deficiency (<30 nmol/l) were reported in 13% (6-24), 54% (41-66), and 33% (22-47) participants, respectively. The mean (SD) vitamin D level was 14.6 (5.0) ng/ml, ranging from 5.3 to 26.9 ng/ml. The median (interquartile range) vitamin D level was 13.5 (11.3-17.3) ng/ml. A comparison of study variables between the vitamin D sufficiency/insufficiency group and the vitamin D deficiency group did not reveal any significant differences (Tables 1 and 2).

Table 1: Comparison of continuous variables between the vitamin D sufficiency/ insufficiency group and the vitamin D deficiency group

Variables	Vitamin D sufficiency/ insufficiency group (≥12 ng/ml) (n = 36) Mean (SD) and Median (IQR)	Vitamin D deficiency group (<12 ng/ml) (n = 18) Mean (SD) and Median (IQR)	p-value
Age (years)	54.8 (12.2) 59.5 (44.8-63.0)	54.9 (10.5) 57.0 (47.3-62.8)	0.80
Duration of stay at Anuradhapura (years)	41.6 (18.9) 41.5 (25.0-58.3)	40.8 (22.4) 47.5 (20.5-58.8)	0.97
Duration of primary hypothyroidism (years)	8.5 (9.4) 5.5 (2.0-10.0)	8.1 (4.9) 7.0 (5.3-9.8)	0.35
Dose of thyroxine (micrograms)	81.9 (35.2) 75.0 (50.0-100.0)	84.7 (32.2) 75.0 (75.0-100.0)	0.68
Hours of sleep per day	7.0 (1.0) 7.0 (6.0-8.0)	6.7 (0.8) 6.5 (6.0-7.0)	0.38
Hours of exposure to direct sun per week	2.3 (5.0) 0.0 (0.0-0.3)	1.1 (4.7) 0.0 (0.0-0.0)	0.11
Weight (kg)	64.9 (12.1) 64.5 (56.7-72.9)	60.9 (10.4) 59.0 (53.9-70.3)	0.24
Body Mass Index (kg/m^2)	26.0 (4.2) 26.4 (23.4-27.8)	26.5 (4.1) 25.7 (24.6-29.3)	0.90

Variables	Vitamin D sufficiency/ insufficiency group (≥12 ng/ml) (n = 36) Mean (SD) and Median (IQR)	Vitamin D deficiency group (<12 ng/ml) (n = 18) Mean (SD) and Median (IQR)	p-value
Waist circumference (cm)	88.8 (10.9) 91.0 (80.8-96.3)	89.3 (9.0) 90.0 (81.3-94.8)	0.95
Hip circumference (cm)	100.9 (8.9) 103.0 (94.0-106.0)	101.1 (8.8) 98.5 (95.5-110.8)	0.99
Waist/Hip ratio	0.9 (0.1) 0.9 (0.8-0.9)	0.9 (0.1) 0.9 (0.8-0.9)	0.97
Pulse rate (per minute)	63.7 (3.5) 64.0 (60.0-64.0)	67.2 (7.0) 64.0 (62.5-72.0)	0.10
Systolic blood pressure (mmHg)	118.1 (11.6) 120.0 (110.0-126.3)	119.7 (12.2) 120.0 (112.5-130.0)	0.59
Diastolic blood pressure (mmHg)	75.1 (8.1) 80.0 (70.0-80.0)	73.3 (6.9) 70.0 (70.0-80.0)	0.32
Pulse pressure (mmHg)	42.9 (7.4) 40.0 (40.0-50.0)	46.4 (8.4) 50.0 (40.0-50.0)	0.08
Mean arterial blood pressure (mmHg)	89.4 (8.8) 93.3 (83.3-96.7)	88.8 (8.1) 90.0 (84.2-96.3)	0.80
Depression score (DASS-21)	7.6 (8.2) 6.0 (2.0-10.0)	10.9 (11.5) 8.0 (2.0-15.0)	0.45
Anxiety score (DASS-21)	8.9 (7.9) 6.0 (2.0-12.5)	13.7 (12.3) 9.0 (4.5-20.5)	0.22
Stress score (DASS-21)	11.5 (8.0) 10.0 (6.0-14.0)	14.4 (11.8) 12.0 (4.5-17.5)	0.60
HbA1C (%)	6.3 (1.3) 5.9 (5.5-6.7)	7.1 (2.2) 6.5 (5.6-7.7)	0.18
Total cholesterol (mg/dl)	169.3 (40.7) 160.5 (141.3-189.0)	189.7 (52.1) 186.0 (147.8-202.8)	0.19
Serum calcium (mg/dl)	8.8 (0.4) 8.8 (8.6-9.0)	8.9 (0.5) 8.8 (8.6-9.0)	0.69
TSH (ng/dl)	3.6 (3.8) 2.5 (1.4-4.2)	2.5 (1.4) 2.5 (1.5-3.8)	0.60
Free T3 (ng/dl)	2.9 (0.7) 2.8 (2.6-3.1)	2.7 (0.4) 2.6 (2.4-2.9)	0.12
Free T4 (ng/dl)	1.3 (0.4) 1.3 (1.1-1.5)	1.4 (0.2) 1.4 (1.3-1.5)	0.46
Estimated GFR (ml/min/1.73m^2)	94.3 (16.1) 98.0 (79.8-105.3)	101.4 (13.2) 102.0 (95.5-111.3)	0.15

Mann-Whitney U test was applied.

Table 2: Comparison of categorical variables between the vitamin D sufficiency/ insufficiency group and the vitamin D deficiency group

Variables	Category	Vitamin D		Logistic regression		
		Sufficiency/ insufficiency group (≥12 ng/ml) (n = 36)	Deficiency group (<12 ng/ml) (n = 18)	Coefficient	p-value	Adjusted odds ratio (95% CI)
Sector of present residence	Urban	09	04	-0.1	0.89	0.9 (0.2 to 4.0)
	Rural	27	14			
Highest educational level	Up to GCE A/L or below	18	10	0.6	0.51	1.8 (0.3 to 9.8)
	GCE A/L completed or above	18	08			
Occupation	Full-time, Part-time	08	05	0.6	0.48	1.8 (0.4 to 9.1)
	Not working	28	13			
Monthly household income (LKR)	≤100,000	17	09	0.1	0.92	1.1 (0.2 to 5.7)
	>100,000	19	09			
Siblings with a history of NCD	Yes	19	11	0.4	0.49	1.5 (0.5 to 5.2)
	No	17	07			

GCE A/L – General Certificate of Education (Advanced Level), LKR - Sri Lankan Rupee

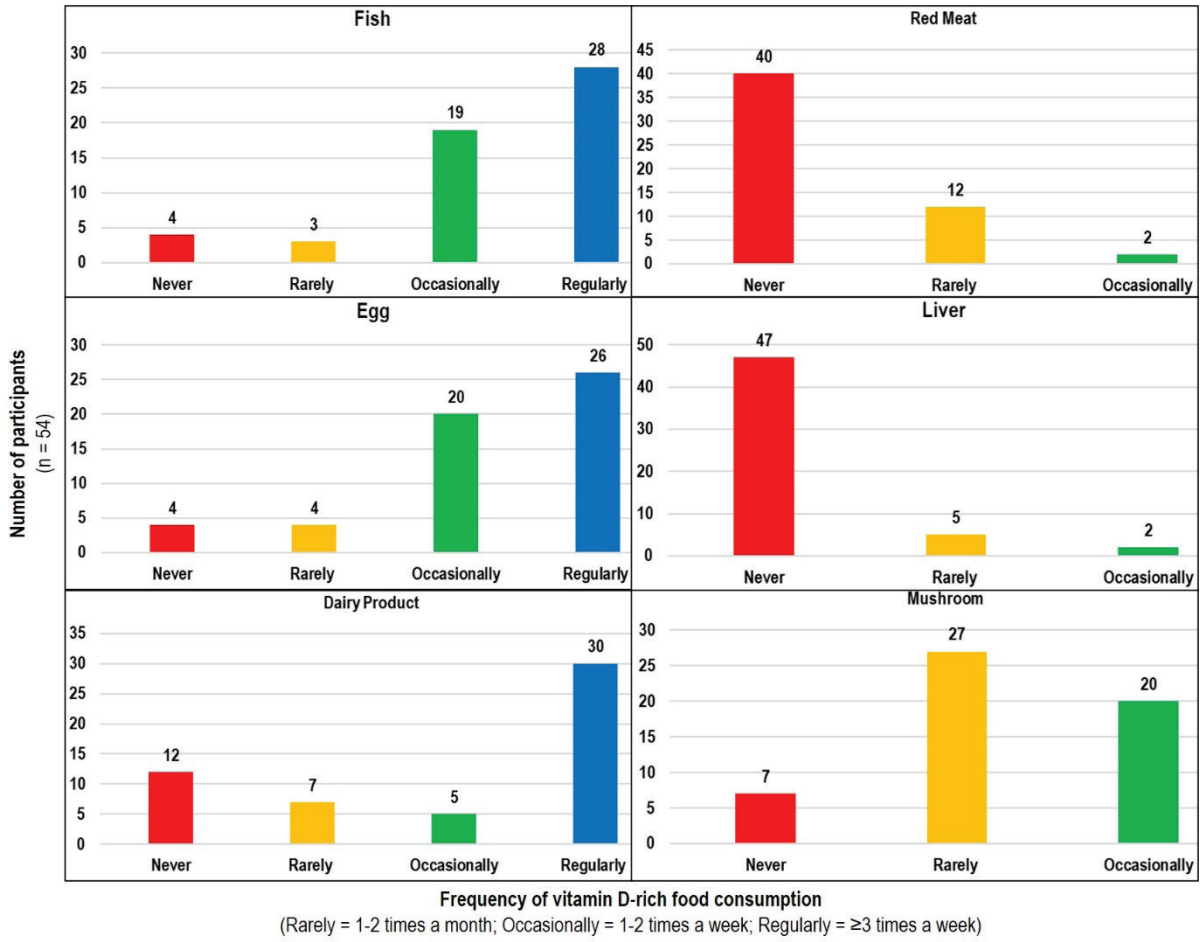

Figure 1: The frequency of vitamin D-rich food consumption among the study participants (n=54).

DISCUSSION

Globally, 15.7% (ranging between 13.7% and 17.8%) and 47.9% (ranging between 44.9% and 50.9%) were reported to have a vitamin D level of <30 nmol/l and <50 nmol/l.[5] A Sri Lankan study done in Colombo urban area found that 58.8% (ranging between 53.5% and 64.1%) had a vitamin D level of <50 nmol/l.[5] However, the present study had 33% (22%–47%) and 87% (76%–94%) participants with <30 nmol/l and <50 nmol/l vitamin D levels among adult patients with primary hypothyroidism in Anuradhapura, Sri Lanka. Hence, a relatively higher percentage of vitamin D deficiency and insufficiency is reported among adult patients with primary hypothyroidism. Previous reports from the United States and South-Asian countries like India and Pakistan have reported similar findings.[2,6,7] Vitamin D has a potential role in the prevention and management of Hashimoto's thyroiditis.[17] Further, the deficiency is correlated with elevated thyroid antibody titers and thyroid cancer.[18] Moreover, supplementation with vitamin D has shown a significant reduction of anti-Tg Ab and TSH hormone.[19]

Vitamin D deficiency is a global health problem which leads to rickets in children and osteopenia, osteoporosis, and fractures in adults.[20] In prior literature, sun exposure score, vitamin D intake, waist-to-hip ratio, and age have been positively correlated, while body fat percentage has an inverse significant association with 25-hydroxyvitamin D among healthy young adults.[21] Moreover, 25-hydroxyvitamin D is reported to be positively correlated with total cholesterol, high-density lipoprotein, calcium, and vitamin B12 levels.[22] Evidence also showed that vitamin D deficiency was found to be associated with being young, female, obese, and having high triglyceride levels in a Sri Lankan population.[5] Apart from that, common cancers, autoimmune diseases, hypertension, and infectious diseases were implicated in vitamin D deficiency.[20] However, a comparison of variables between the vitamin D

sufficiency/ insufficiency group and the vitamin D deficiency group did not reveal any significant differences.

The findings of a preliminary cross-sectional study from a single geographical area cannot be generalised, nor can they establish a causal association. Additionally, the preliminary nature and limited funding precluded a comparison of findings among patients with other chronic diseases or healthy volunteers. Future large-scale comparative studies among adult patients with primary hypothyroidism, other chronic diseases and healthy volunteers are necessary for confirmation of the prevalence, its significance and associated factors for vitamin D deficiency. Nevertheless, the present findings from Anuradhapura, Sri Lanka, are unique and provide useful baseline information for future related studies.

CONCLUSION

The preliminary study reports the prevalence of vitamin D deficiency among adult patients with primary hypothyroidism in Anuradhapura, Sri Lanka. Vitamin D insufficiency and deficiency were reported in 54% and 33%, respectively. The findings provide an important lead for healthcare officials, practitioners, and future large-scale studies. Similar studies among patients with other chronic diseases and healthy volunteers are proposed for comparison.

Conflict of interest: None declared by the author.

Funding statement: The study was partially funded by the grant awarded by the Research and Publication Committee, Rajarata University of Sri Lanka (Grant No. RJT/R&PC/2025/R/FMAS/07) for laboratory analysis and stationery costs. However, the above agents did not influence the design of the study, collection, analysis and interpretation of data or the writing of the manuscript.

Ethical approval: Ethical clearance was obtained from the Ethics Review Committee of the Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka (ERC/2025/11). Prior permission was obtained from the Regional Director of Health Services, Anuradhapura, Sri Lanka. and the selected pharmacy, The pharmacy outlet served only as a referral point, providing the names, ages, genders and phone numbers of patients willing to participate in the study. No data collection took place at the pharmacy premises. Written informed consent was taken from each participant. Their anonymity and data confidentiality were strictly maintained.

Author's contribution: The author was solely responsible for concept, design, patient selection, data collection, compilation and analysis as well as manuscript preparation, editing and final submission.

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