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ARTICLE

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Status of serum vitamin D and neurological disorder in Nepalese population: a prospective study

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Abstract

Background: Recently, there has been a surge in research worldwide on vitamin D. based on international level, Vit. D has shown positive correlation with cardio-cerebrovascular disorders. Regarding possible role of vitamin D there is paucity of research in low- and middle-income nations that are nearer to the equatorial area. Despite of abundant sunlight exposure, Asian people are developing hypovitaminosis D need a special consideration to avoid excessive and unnecessary usage of it. This study aims to detect the situation of vitamin D in Nepalese population and secondly to find out the suitable normalized reference range for serum vitamin D in multi-ethnic Nepalese population. **Methods:** A hospital based prospective study was conducted using purposive sampling technique to select 107 subjects. In-vivo and in vitro bio-physiological method was used to collect serum vitamin D level. **Result:** The present study showed that 32% of participants had deficit (< 15 ng/mL), 48% of subjects had insufficient (15 to < 30 ng/mL) and 20% of participants had sufficient serum level of Vitamin-D (> 30 ng/mL). Study showed that there is a lower degree of positive relationship of body mass index ($r = 0.162$, $P = 0.094$) and significant association of history of chronic illness ($\chi^2 = 0.10$, $P = 0.03$), timing of occurrence of stroke ($\chi^2 = 11.41$, $P = 0.017$) and diagnosis ($\chi^2 = 21.19$, $P = 0.011$) with serum vitamin-D level at $P < 0.05$. **Conclusion:** There is a direct significant association of serum vitamin D with socio-demographic variables when international unit is considered. Neurological disorder showed positive association with serum vitamin D level.

Key words: Serum vitamin D, Neurological disorder, Deficiency, Incidence

Abbreviations:
DALYs, disability-adjusted life year; BMI, basal metabolic index; RR, relative risk; OR, odd ratio; hs-CRP, high-sensitivity C-reactive protein.

Competing interests:
The authors declare that they have no conflict of interest.

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Background

Research of vitamin D in neurology has gained momentum recently. Many neurological ailments like multiple sclerosis [1], spinal diseases, Alzheimer's disease [2] as well as other diseases like cardiovascular disease [3] have shown positive correlation with vitamin D deficiency. Probably this is one of the main reasons that family physicians and neurologists have opted for including serum vitamin D in their lab investigation. However, the reference range that is followed in all over the world comes from the western world consisting of data largely based on the Caucasian population and measurement and clinical interpretation is done on the basis of this reference level [4, 5]. Vitamin D is a group of fat-soluble prohormones which were identified after the discovery of the anti-rachitic effect of cod liver oil in the early part of the 20th century. The 2 major biologically inert precursors of vitamin D are vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol). Both vitamin D precursors resulting from exposure to the sunshine and the diet are converted to 25-hydroxyvitamin D [25(OH)D] (calcitriol) when they enter the liver. 25(OH)D is the major circulating form of vitamin D and is used to determine vitamin D status vitamin D has several roles in the body, including modulation of cell growth, neuromuscular and immune function, and reduction of inflammation. Many genes encoding proteins that regulate cell proliferation, differentiation, and apoptosis are modulated in part by vitamin D [6, 7].

Despite the numerous studies about the association between vitamin D and different health outcomes, there are still controversies defining the adequate vitamin D status, daily intake needed and the potential adverse health consequences of its deficiency or toxicity. Serum 25-hydroxy vitamin D concentrations are being used to define vitamin D deficiency, but the diagnostic test accuracy of these measurements and the reference standard used are not clearly stated. There appears to be wide variability between different essays for its determination in different laboratories and there is not yet international consensus on the optimal concentrations in different population groups [8]. According to the epidemiologic studies, based on the internationally accepted serum vitamin D levels, about 1 billion people worldwide have vitamin D deficiency, while 50% of the population has vitamin D insufficiency [9]. The prevalence of patients with vitamin D deficiency is highest in the elderly, the obese patients, nursing home residents, and hospitalized patients. Prevalence of vitamin D deficiency was 35% higher in obese subjects irrespective of latitude and age [10].

In South-Asian region 80% of the healthy population is deficient in vitamin D and up to 40% of the population is severely deficient when considered according to the international level [11]. A study on hypovitaminosis D in developing countries to assess prevalence, risk factors and outcomes revealed that though South Asia region has ultra violet B radiation levels that are sufficient for vitamin D synthesis for 11 to 12 months of the years, however, serum 25-hydroxyvitamin D levels of < 25 nmol/L have been reported in more than 50% of the infant, children and women [12]. Another study conducted on prevalence of Vitamin D deficiency among adult patients in a tertiary care hospital in Nepal has reported that out of total patients, vitamin D deficiency was found among total of 283 patients. Vitamin D deficiency was found to be higher in females than males [13]. In spite of lavish sunlight over 300 sunny days a year [14] and no cultural avoidance of sun several data have reported poor vitamin D status. As people have adopted an urban life style they tend to stay at home a lot, less intake of dietary sources such as oily fish, mushrooms, sea food etc., pregnancy, critical illness can be the reason of hypovitaminous D in Nepal [15].

Neurological disorders are an important cause of disability and death worldwide. Globally, the burden of neurological disorders has increased substantially over the past 25 years because of expanding population numbers and growing ageing, despite substantial decreases in mortality rates from stroke and communicable neurological disorders [16]. A systemic analysis for global, regional and national burden of neurological disorders during 1990–2016 stated that globally, in 2016, neurological disorders ranked as the leading cause of disability-adjusted life year (DALYs) in 2016 (i.e. 276 million, comprising 10.2% of global DALYs) and second-leading cause group of deaths (i.e. 9 million, comprising 16.8% of global deaths). The 4 largest contributors of neurological DALYs were stroke (42.2%), migraine (16.3%), Alzheimer's and other dementias (10.4%) and meningitis (7.9%) [17]. As considerable hypovitaminosis D is common in Asians, physicians often prescribe cholecalciferol at a dose of 60,000 IU/week for 2 months, then at 60,000 IU/month for 6 months for occult vitamin D deficiency [18]. Although this practice is most commonly followed, the adverse effects on excessive supplementation of vitamin D and the high serum 25(OH)D levels in Nepalese individuals have not been systematically studied.

Some recent studies are contradicting with previous studies as they explain negative effects of vitamin D supplementation. Because of growing awareness of vitamin D deficiency and related health problem, vitamin D has become a popular supplement. The typical regimens of vitamin D Supplementation i.e. 1,000IU to 2,000 IU twice monthly might be harmful to bone quality and strength [19]. Excess intake of vitamin D or hypervitaminosis D may leads to toxicity, hypercalciuria, hypercalcemia and increased bone

absorption [20]. In a placebo controlled trial, high dose once yearly vitamin D therapy with subsequent 25(OH)D levels > 30 ng/mL led to a higher number of fractures and falls [21]. The serum 25(OH)D levels > 30 ng/mL are not necessary nor optimal for all individuals [22].

Notably, serum vitamin D is inconsistent in diverse population. Even in the homogenous population of Caucasians, vitamin D genetic variability in vitamin and calcium receptors has been witnessed [23, 24]. In countries like Nepal, geographically they lie near to the equator and sunlight exposure is well enough. Thus, special consideration for vitamin D level in Asian population seems plausible. This will not only help us to cover the vitamin D deficient population [25, 26], but will also help us to avoid excessive and unnecessary usage of it. We have sought to find out whether the depletion of vitamin D in our population is for real and if these are of real, does the depletion vitamin D cause the neurological disorders?

Methodology

Population

The purpose of the study was to find out the suitable normalized reference range for serum vitamin D in multi-ethnic Nepalese population and to detect the correlation of vitamin D and neurological disorders. The quantitative research design was selected for the dependent variables i.e. serum Vitamin D level and independent variables i.e. health history, history of chronic illness, types of stroke, smoker and alcohol consumption, physical activity and basal metabolic index (BMI) of subjects, socio-demographic variables such as age, sex, education, marital status and address of subjects. Prospective purposive sampling technique was used. A total of 108 subjects were included. The sample size was determined using Yamane (1967) simplified formula [27], where level of precision was 0.0654. The study was approved by institutional review board of our institute and informed written consent was obtained from each participant (Supplementary Material 1). The data collection was conducted from 1st September till 1st January. Inclusion and exclusion criteria were set as the inclusion criteria for present study was the subject with: a) age 18 years and older, b) anyone willing to take part & c) presence of any neurological disease and d) any healthy person present at the time of data collection. Exclusion criteria were: a) age below 18 years or above 90 years, b) not giving consent, c) no other chronic illness besides neurological (diabetes, other cancers, gynecologic diseases, hypertension and d) anyone taking calcium or vitamin concentrates or supplements or has been treated for calcium recently or vitamin D supplements (within 30 days).

Clinical examination

The socio-demographic variables were measured using structured questionnaire that consists age, sex, educational status, permanent address, marital status of subjects. The part of same questionnaire consisted personal history such as history of stroke, type of stroke, chronic illness, physical activity, smoking habits, and alcohol consumption. All the subjects were examined with physical and neurological examination by experienced physician, and neurologist. In-vivo bio-physiological method was used to measure BMI and in-vitro bio-physiological method was used to quantify level of vitamin-D using enzyme-linked immuno-sorbent assay method with 'Mono Bind Inc.' USA. Radiological measurements were also performed to confirm the neurological disorders. BMI, formerly called the Quetelet index, is a measure for indicating nutritional status in adults is defined as a person's weight in kilograms divided by the square of the person's height in metres (kg/m^2). The level of BMI was distributed as a) < 18.5 kg/m^2 under-weight, b) 18.5–24.9 kg/m^2 normal weight, c) 25–29.9 kg/m^2 over weight and d) >3 0 kg/m^2 obesity [21]. In another hand the level of vitamin-D was scored as a) < 15 ng/mLdeficit, b) 15 to < 30 ng/mL insufficient and c) > 30 ng/mL sufficient.

Statistical analysis

Statistical analysis was performed using the IBM Statistical Package for the Social Sciences (SPSS version 20). A descriptive analysis: frequency, percentage, mean, and standard deviation were used to describe the socio-demographic variables and independent variables. An inferential analysis: Chi-square test, Karl Pearson correlation coefficient, multivariate linear regression analysis was used to find association between level of vitamin-D and selected socio-demographic variables and independent variables of Nepalese people. A nominal P-value of ≤ 0.05 was considered statistically significant, and P < 0.1 was considered a trend, using two-tailed test.

Results

Demographic and clinical characteristics

The collected data were analyzed and interpreted based on research objectives. The demographic characteristics of total 108 eligible subjects are presented in Table1.1, among them more than half i.e. 66% (71) were male, one third of subjects i.e. 36% (39) were 46–60years old age group, majority of participants i.e. 76% (82) were from hilly region, more than half of subjects were i.e. 62% (67) from inside the Kathmandu valley (capital of Nepal). With regards to education 44% (48) had received only primary education level (spent few years in school), 89% (96) participants were married. Majority of the participants i.e. 71% (77) were active in

TMR
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Table 1.1 Characteristics of the study population (n = 108)

	Frequency (%)	Mean ± SD
Sex		
Male	71 (65.7)	
Female	37 (34.3)	
Age		61.100 ± 14.920
< 45 years	16 (14.8)	
46–60 years	39 (36.1)	
61–75 years	33 (30.6)	
> 75 years	20 (18.5)	
Marital status		2.110 ± 0.316
Married	96 (88.9)	
Unmarried	12 (11.1)	
Address		1.940 ± 0.490
Terai/plain region	16 (14.8)	
Hilly region	82 (75.9)	
Mountain region	10 (9.3)	
Education		1.810 ± 1.148
Illiterate	8 (7.4)	
Primary	48 (44.4)	
Secondary	20 (18.5)	
Intermediate	21 (19.4)	
Others	11 (10.3)	
Physical activity		1.290 ± 0.454
Active	77 (71.3)	
Inactive	31 (28.7)	
Smoke		1.720 ± 0.450
Smoker	30 (27.8)	
None smoker	78 (72.2)	
Alcohol		1.710 ± 0.454
Alcoholic	31 (28.7)	
Non alcoholic	77 (71.3)	

their life, 28% (30) were smokers and 29% (31) were alcohol consumer. Among the participants, 40% (43) had stroke, among which, more than half 58% (63) had approached emergency department in less than 24 hours of stroke onset. Presented in Table 1.2 majority of subjects i.e. 75% (81) had chronic illness with hypertension and other condition; similarly, 72% (78) of participants were suffering with chronic illness since less than 5 years. With regards to types of stroke, 64% (69) and 36% (39) had ischemic and hemorrhagic stroke, respectively.

Incidence of serum vitamin D in Nepalese population and its relationship with BMI

The status of serum vitamin-D has been presented in Table 2. The present study showed that 32% (34) of participants had deficit serum Vitamin-D level (< 15 ng/mL), 48% (52) of subjects had insufficient serum level of vitamin-D (15 to < 30 ng/mL) and 20% (22) of participants had sufficient serum level of vitamin-D (> 30 ng/mL). Majority of participants i.e. 73% (79) had normal body weight, 22% (24) of subjects had overweight, 2.8% (3) were obese and 0.9% (1) was under weight. The current study stated that there is lower degree of positive relationship of BMI with serum vitamin-D level (r = 0.162, P = 0.094), that is statistically not significant at $P < 0.05$. In another way there is no statistically significant association between BMI and vitamin D (χ^2 = 12.474, P = 0.071).

Serum vitamin-D level and association with socio-demographic variables and clinical characteristics

Table 3 states the association between serum vitamin-D level and socio-demographic variables. Present study revealed that serum vitamin-D level was significantly associated with gender (χ^2 = 0.233, P = 0.003), marital status (χ^2 = 0.562, P = 0.014), address (i.e. Terai which means plain low land of Nepal, hilly and mountainous region) (χ^2 = 4.431, P = 0.009) and physical activity (χ^2 = 0.193, 0.013). Whereas, there was lower degree of negative relationship of serum vitamin D with gender (r = 0.045, P = 0.649), marital status (r = 0.015, P = 0.88) and positive relation with physical activity (r = 0.111, P = 0.25) and address (r = 0.12, P = 0.27). With regards to history of chronic illness (χ^2 = 0.10, P = 0.03), timing of occurrence of stroke (χ^2 = 11.41, P = 0.017) and diagnosis (χ^2 = 21.19, P = 0.011), there was significant association with serum vitamin-D level at P <0.05. There was lower degree of positive relation of chronic illness (r = 0.053, P = 0.579) and diagnosis (r = 0.012, P = 0.902) with serum vitamin-D level. We also observed a poor level of positive relation of smoker (r = 0.02, P = 0.805) and alcoholism (r = 0.059, P = 0.534) with serum vitamin D level, but statistically not significant. Smoke (χ^2 = 0.355, P = 0.048) was significantly associated with serum level of vitamin-D. The serum vitamin-D level was not significantly associated with age (χ^2 = 0.64, P = 0.09), educational status (χ^2 = 11.54, P = 0.21), history of stroke (χ^2 = 11.62, P = 0.06) and type of stroke (χ^2 = 4.84, P = 0.21) at P = 0.05.

Discussion

Vitamin D deficiency has been mechanistically and clinically linked to neurological diseases and neuropsychological disorders, cognitive impairment, and neurodegenerative diseases [28]. Our current study has emphasized that 32% of participants had deficit serum vitamin-D level, 48% of subjects had insufficient and 20% of participants had sufficient serum level of vitamin-D. Studies carried across different countries in South and South East Asia showed, with few exceptions, widespread prevalence of hypovitaminosis D, in both sexes and all age groups of the population [29]. High prevalence of hypovitaminosis D in South Asia can be explained by skin pigmentation and

Table 1.2 Clinical characteristics of the study population (n = 108)

	Frequency (%)	Mean ± SD
Diagnosis		5.780 ± 2.670
Thalamic hemorrhage	14 (13.0)	
MCA infract	6 (5.6)	
Basal ganglia ischemia	7 (6.5)	
Basal ganglia infraction	4 (3.7)	
Basal ganglia hemorrhage	17 (15.5)	
Right sided parietal ischemia	10 (9.3)	
Left sided parietal ischemia	34 (31.5)	
Multi infract	6 (5.6)	
Other ischemia	2 (1.9)	
None	8 (7.4)	
Health history at the time of admission		2.360 ± 1.670
Right sided weakness	38 (35.2)	
Left sided weakness	43 (39.8)	
Blurred vision	4 (3.7)	
Loss of consciousness, dizziness & headache	9 (8.3)	
Slurred speech	8 (7.4)	
Unable to recall & disorientation	1 (0.9)	
Bilateral weakness & ABM	3 (2.8)	
Healthy	2 (1.9)	
Types of stroke		1.360 ± 0.480
Ischemic stroke	69 (63.9)	
Hemorrhagic stroke	39 (36.1)	
Timing of stroke before admission		1.590 ± 0.830
<1 day	63 (58.3)	
1–5 days	31 (28.7)	
6–10 days	9 (8.3)	
11–15days	5 (4.6)	
History of chronic illness		0.750 ± 0.420
Hypertension	27 (25.0)	
Hypertension and other	81 (75.0)	
Timing/length of chronic illness		1.410 ± 0.789
0–5 years	78 (72.2)	
6–10 years	21 (19.4)	
11–15 years	5 (4.6)	
6–20 years and more	4 (3.7)	

Table 2 Prevalence of serum vitamin D and BMI among Nepalese population (n = 108)

	Frequency (%)	Mean ± SD
Level of serum vitamin-D		21.85 ± 13.57
< 15 ng/mL deficit	34 (31.5)	
15 to < 30 ng/mL insufficient	52 (48.1)	
> 30 ng/mL sufficient	22 (20.4)	
Level of BMI		23.63 ± 2.83
< 18.5 Kg/m^2 under weight	2 (1.8)	
18.5–24.9 Kg/m^2 normal weight	79 (73.1)	
25–29.9 Kg/m^2 over weight	24 (22.2)	
> 30 Kg/m^2 obesity	3 (2.8)	

BMI, body mass index.

traditional clothing. Air pollution and limited outdoor activity further compounds this problem in the urban population [30]. The pluralistic, multireligious and mosaic culture of Nepalese society has adopted and adjusted with the cumulating onslaught of western life style. Even though 93% of the population live in rural areas are no longer beset with old aged culture and social tradition [31]. The current study stated that

TMR
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Table 3 Association of vitamin-D with socio-demographic variables (n = 108)

	Chisquare (χ^2)	*P*-value	Karl-pearson coefficient correlation (r)	*P*-value
Sex	0.23#	0.003	−0.045*	0.65
Age	0.64	0.090	0.039	0.68
Marital status	0.56#	0.014	−0.015*	0.88
Address	4.43#	0.009	0.120	0.27
Education	11.54	0.210	−0.183*	0.06
Physical activity	0.19#	0.013	0.111	0.25
Smoke	0.36#	0.048	0.020	0.81
Alcohol	4.12	0.189	0.059	0.53
Diagnosis	21.19#	0.011	0.012	0.90
History of stroke at the time of admission	11.62	0.060	0.032	0.22
Types of stroke	4.84	0.210	−0.121*	0.21
Timing of stroke before admission	11.41#	0.017	0.032	0.24
History of chronic illness	0.10#	0.030	0.053	0.58
Timing/length of chronic illness	8.07#	0.120	0.115	0.24
BMI	12.47	0.071	0.162	0.09

BMI, body mass index. #, significantly associated; *, negative relation.

there is lower degree of positive relationship of BMI with serum vitamin-D level ($r = 0.162$, $P = 0.094$), that is statistically not significant at $P < 0.05$. In another way there is no statistically significant association between BMI and vitamin D ($\chi^2 = 12.474$, $P = 0.071$). The finding is supported by a study on the effect of vitamin D supplementation on serum 25-OHD in thin and obese women as the result showed a significant inverse relation between total body fat mass and serum 25-OHD ($P < 0.0001$) and serum $1,25(OH)_2D$ ($p = 034$). There was no significant change in total body fat mass after treatment with vitamin D or calcitriol in randomized trials [32]. Similarly the finding is contradicted by the study aimed to find association between BMI and vitamin D supplement the result stated that there was significant differences in mean 25-OHD levels of vitamin D supplementation doses were consistently seen across BMI categories [33]. Again contradicted by another cross-sectional study on serum vitamin D level in different 222 socio-demographic population The mean difference between normal and obese population was statistically significant ($P = 0.007$) [34].

Present study revealed that serum vitamin-D level was significantly associated with gender ($\chi^2 = 0.233$, $P = 0.003$), marital status ($\chi^2 = 0.562$, $P = 0.014$), address (i.e. Terai, Hilly and mountain region) ($\chi^2 = 4.431$, $P = 0.009$) and physical activity ($\chi^2 = 0.193$, 0.013). Several national and international previous studies supported the finding as an ecological study conducted to assess association of vitamin D status with socio-demographic factors in Calgary, Canada, result of the study revealed that there is significant association between 25-hydroxyvitaminD level and all the predictors i.e. age, gender and educational status (all $P < 0.0001$) [35].Another study on determinants of vitamin D status in young adults; influence of lifestyle, sociodemographic and anthropometric factors among 738 subjects revealed that the relative risk (RR) for vitamin D deficiency was highest for men 2.09 (1.52, 2.87); subjects who exercised 0–½ hours a week 1.88 (1.21, 2.94) [36]. A study aimed to assess the association between vitamin D deficiency and depression in Nepalese population stated significant association of gender, geographical location of residence, marital status, religion and vitamin D status with clinically significant depression [37]. Other study has been observed a direct relationship between latitude and the prevalence of multiple sclerosis (MS), which suggests a role for UV radiation and vitamin D in MS development [38].

There was poor level of positive relation of smoker ($r = 0.02$, $P = 0.805$ and alcoholism ($r = 0.059$, $P = 0.534$) with serum vitamin D level, but statistically not significant. Smoke ($\chi^2 = 0.355$, $P = 0.048$) was significantly associated with serum level of vitamin-D whereas no association of alcohol with vitamin-D level at $P < 0.05$. A cross-sectional study on determinants of vitamin D status in young adults; influence of lifestyle, sociodemographic and anthropometric factors among 738 subjects supports as the result of study revealed that 238 subjects had vitamin D insufficiency, 135 had vitamin D deficiency of which 13 had severe vitamin D deficiency (S-25[OH]D < 12.5 nmol/L). The RR for vitamin D deficiency was highest for smokers 1.33 (1.02, 1.73). Smoking was associated with a higher *RR* = 1.33 (1.02, 1.73) for vitamin D deficiency compared with nonsmoking. Whereas contradicted the result of alcohol as alcohol intake was associated with a lower *RR* = 0.68 (0.47, 0.90) for vitamin D deficiency compared to non-drinker, an increase of one unit of

alcohol was associated with *RR* = 0.81 (0.68–0.97) [36]. Another study on interaction of vitamin D and smoking on inflammatory markers, the data was collected from Korean Elderly Environmental Panel Study that included 560 subjects. The result of the study was that association of vitamin D deficiency and high-sensitivity C-reactive protein (hs-CRP) in smokers was stronger than that in nonsmokers (smokers: $\beta = -0.375$, $P = 0.013$; non-smokers: $\beta = -0.060$, $P = 0.150$). Smoking status was an effect modifier that changed the association between vitamin D deficiency and hs-CRP (interaction estimate: $\beta = -0.254$, $P = 0.032$). There was a stronger significant association of smokers and vitamin D deficiency than non-smokers [39]. A review on vitamin D and alcohol aimed to evaluate the association between alcohol use and vitamin D serum levels alcohol intake was found to be positively associated with vitamin D status in 15 articles and negatively associated with vitamin D in 18 articles [40]. The finding is contradicted by another study on chronic ethanol exposure effects on vitamin D levels among subjects with alcohol use disorder stated that levels of inactive vitamin D ($25(OH)D_3$), active vitamin D ($1, 25(OH)_2D_3$), cathelicidin/LL-37, and CYP27B1 proteins were significantly reduced ($P < 0.05$). Chronic exposure to alcohol has the potential to reduce the levels of vitamin D [41].

Several evidence suggests that vitamin D acts like a neurosteroid and is required for normal brain development and function [42]. An endocrine review on vitamin D and neurological diseases, aimed to highlight the relationship between vitamin D and neurological diseases stated that there is association between low levels of 25(OH)D and a wide spectrum of neurodegenerative conditions such as multiple sclerosis, Alzheimer's disease, Parkinsons's disease and neurocognitive disorders, is supported by in vitro and in vivo data [43]. Other studies showed that the risk of MS decreases with increasing intake of vitamin D [44], and serum 25(OH)D levels are significantly lower in patients with MS as compared to healthy controls [45]. These studies directly support the results of our current study as history of chronic illness ($\chi^2 = 0.10$, $P = 0.03$), timing of occurrence of stroke ($\chi^2 = 11.41$, $P = 0.017$) and diagnosis ($\chi^2 = 21.19$, $P = 0.011$) had significant association with Serum vitamin-D level at $P < 0.05$. There was lower degree of positive relation of chronic illness ($r = 0.053$, $P = 0.579$) and diagnosis ($r = 0.012$, $P = 0.902$) with serum vitamin-D level. Whereas the serum vitamin-D level was not significantly associated with History of stroke ($\chi^2 = 11.62$, $P = 0.06$) and type of stroke ($\chi^2 = 4.84$, $P = 0.21$) at $P = 0.05$.

Another cross-sectional study to evaluate the association between vitamin-D and hypertension among 520 people supports the study as the result stated that Severe vitamin D deficiency was highly prevalent in people with hypertension than in people without hypertension (P value < 0.001). The study concluded that vitamin D deficiency was associated with an increased risk of having hypertension [46]. In our current study subjects 25% (27) had chronic illness history with hypertension and the Karl pearson correlation coefficient showed positive relation as well significant association with serum vitamin D level of Nepalese residents. A Similar case-control study aimed to assess the serum level of vitamin D in cerebral stroke patients and secondly, to examine if its deficiency was associated with stroke severity and outcome result revealed that studied stroke patients had statistically significant lower levels of vitamin D. Multivariable analysis of the significant variables showed that old age (odd ratio (OR) = 1.072), dyslipidemia (OR = 3.588), vitamin D deficiency (OR = 4.790), and large infarction size (OR = 7.462) was independently associated with stroke severity. The study concluded that stroke patients suffer from vitamin D deficiency, which was associated with both stroke severity and poor outcome [47].

A study on reduced vitamin D in acute stroke compared the serum 25-dihydroxyvitamin D levels with first-ever stroke the result revealed no relationship between 25OHD level and the length of time between stroke and 25OHD sampling (adjusted $r^2 = -0.02$; $P = 0.77$). The mean Z score of vitamin D in acute stroke was −1.4 SD units (95% CI, −1.7, −1.1), with 77% of patients falling in the insufficient range concluded that reduced vitamin D was identified in the majority of patients with acute stroke throughout the year and may have preceded stroke [48]. A vitamin D deficiency and incident stroke risk in community living black and white, supports the finding as the study revealed there was no statistically significant differences in the association of lower 25-hydroxyvitamin D with higher risk of stroke in black i.e. (95% CI, 1.18, 5.83) vs. white i.e. (95% CI, 0.83, 3.24) participants [49]. Another study on vitamin D in amyotrophic lateral sclerosis represented that in chronic neurological diseases levels of vitamin D in blood appeared low but there was no significant differences found between the level of vitamin D and amyotrophic lateral sclerosis patients (18.8 ± 12.2) and the healthy subjects (20.7 ± 10.1) [50]. Similarly, cross-sectional associations of plasma vitamin D with cerebral β-amyloid in older adults at risk of dementia, the study didn't find the association between baseline 25(OH)D levels and cerebral Aβ in any of the brain regions studied [51]. Vitamin D is not associated with incident dementia or cognitive impairment over an 18 years period of time another study presented as the result showed that the adjusted hazard ratio for the continuous Gibbons Ross shanken for all cause dementia was 1.04 (95% CI: 0.91, 1.19) [52]. A study to investigate association between serum concentration of vitamin D and 1-year mortality in stroke patients presents that out of the 382 stroke patients, 16.5% died in a year, and the mean 25(OH)D

TMR
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level was lower in those patients (32.3 ± 22.0 vs. 44.6 ± 28.7 nmol/L, $P < 0.001$) and survival at 1 year was worse in patients in the lowest tertile of 25(OH)D levels (i.e. < 25.7 nmol/L). The study concluded that low level serum 25(OH)D level at stroke onset association was with higher mortality at 1 year in patients [53]. The finding from this study may supports for the implementation of measures to determine the real state of vitamin D and its implication on Neurological disorders. We recognize some limitations of our study as the study completed with small size of 108 due to rigorous inclusion and exclusion criteria. As it was a hospital-based study, sample might not be enough to represent the total population of our country. The study should be continued with similar control groups.

Conclusion

Despite abundant sunlight in Nepal several studies suggest the prevalence of vitamin D deficiency in this region. Our question is whether the reference given globally is accurate for the land-locked country with different geographical area, multi-cultural, religion and practices. Through the study we concluded that more than half of population having serum vitamin-D insufficiency. Level of serum vitamin-D is significantly associated with socio-demographic variables as well with neurological conditions but there are lots of caveats with it. A larger population-based study in multinational (equatorial region) seems necessary.

Ethics approval

The study was conducted after proper approval obtained from the ethics review committee and Institutional Review Board of ANIAS (approval letter submitted as a supplementary material).

Consent to participate

The participants were well informed about the study. The participants were well informed in written and well explained and obtained consent to participate.

Availability of data and materials

The availability of data and materials is provided in supplementary file.

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