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Frequency of Low Vitamin D3 Levels in Subjects with Parkinson's Disease. A Study Conducted at PMCH, a Tertiary Care Hospital, Nawabshah

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Abstract

Background: Lack of serum vitamin D3 is related to PD (Parkinson's disease). Currently a valid place for vitamin D3 deficiency in Parkinson disease (PD) has been anticipated. The aim of present research was to evaluate insufficiency of D3 (vitamin) in subjects with PD (Parkinson's disease). Many of physiological functions connected with higher risk of illness are maintained by vitamin D, which also plays significant task in pathogenesis of calcium homeostasis and skeletal ailments. It forecasts hazard of persistent ailments like malignancy, CVS conditions, and T2DM. Continuous insufficiency of this vitamin may lead to PD. **Method:** This was a cross sectional study. Conducted at People's Medical College Hospital, Nawabshah during period of Jan. 2014-Dec. 2016, the sample size of 243 subjects clinically diagnosed as PD was enlisted. Inclusion criteria were all male and female subjects aged >50 years, clinically diagnosed Parkinson's disease enlisted in research. **Results:** In 151 (62.1%) subjects, vitamin D3 levels were <30 ng/ml while in 92 (37.9%) subjects, vitamin D3 values were normal (30 - 150 ng/ml) ($p = 0.000$). **Conclusion:** Considerably low levels of vitamin D3 were seen in Parkinson's disease. Our information sustains a legitimate part of vitamin D insufficiency in PD.

Keywords

Parkinson's Disease, Vitamin D Deficiency, Nawabshah

1. Introduction

Vitamin D, a fat-soluble vitamin, has many biological consequences. It increases absorption of calcium, phosphate and magnesium in gut. Vitamin D3 and D2 (Cholecalciferol, Ergocalciferol) are essential compounds in our body [1]. Parkinson's Disease is widespread neurological ailment of old age with unidentified cause. PD has great financial burden and social status of people universally. Uneven prevalence and incidence rates may be affected by ecological or hereditary components, approaches for case determination, diagnostic criterion, or age disseminations of investigation populaces may affect outcomes. Equivalence of existing researches is restricted [2]. Vitamin D3 assumes a critical part in pathogenesis of skeletal ailments and calcium homeostasis [3]. Vitamin D insufficiency likewise predicts expanded danger of other perpetual ailments, malignancy, [4], cardiovascular sicknesses [5] and DM (type 2) [6]. Constantly deficient vitamin D values promote a constant loss of dopaminergic neurons and propose to assume a major part in the pathogenesis of PD [7]. The epidemiological confirmation of a relationship among vitamin D and PD is, however, constrained to cross-sectional researches [8] [9] [10].

Studies had declared that in America (North), hundreds of populations who suffer from PD are vitamin D deficient. There is connection among PD and D3. These results have a strong correlation in old age peoples and fall risks and intimates additional search into the method essential for this connection [11]. Subjects with PD have decreased vitamin D concentrations in relation to controls. PD is a noteworthy reason for incapacity in older people. Biological credibility and epidemiological information show that vitamin D inadequacy may add to PD progression [7]. The recent research explored whether D3 level predicts Parkinson disease occurrence in populace of Pakistan where solar exposure is high from different zones of world. Vitamin D inadequacy had turned into universal issue in the older, kids and grown-ups [12] [13]. Lack of vitamin D3 can occur from decreased solar contact [14]. Altered bone mineralization and bony injury are associated with insufficiency leading to softening bony ailments (osteomalacia and rickets) [15] [16]. This study will help in future to manage PD patients properly by reducing risk, treating and avoiding complications by giving additional supplements of vitamin D as a primary step by adding the basic element to diet and as drug.

2. Methods

2.1. Subjects and Setting

A sum of 243 diagnosed PD subjects from local community enrolled during 2014 to 2016 attending Department of Medicine, People's Medical University Hospital Nawabshah, Sindh, Pakistan. Sample size calculated by OpenEpi version 3, with population size 1.6 million, hypothesized percent frequency of outcome factor in PD 66/100,000, with confidence level 90% and margin of error 10%. Subjects with other neurodegenerative, thyroid ailments, and new change in life-

style or nutritional status excluded. A questionnaire based interview and complete clinical examination performed in subjects. All aspects of research updated to subjects and signed consent obtained. Educational situation, routine daylight contact, cigarettes, alcohol, head injury, pesticide exposure and medical history taken by direct questions. This study conducted after authorization of Peoples Medical University Hospital ethical committee.

2.2. Diagnoses of PD and Vitamin D3 Deficiency

Parkinson's disease was diagnosed through UK PD Society Brain Bank clinical diagnostic criteria, [17] clinical history and relevant signs on examination of patients. Vitamin D3 deficiency diagnosed through laboratory analysis of blood samples of PD sufferers. Serum 25(OH)D concentrations > 30 ng/ml normal, >20 and <30 ng/ml insufficiency and deficiency < 20 ng/ml [18].

A well-versed printed consent dully signed by subjects with diagnosis of PD obtained and gratifying inclusion criterion attending Medical Departments PMC Hospital Nawabshah. The venous blood drawn, sent to laboratory for analysis of serum Vitamin D3 by Mini Vidas Biomerieux Global Company France. Levels < 30 ng/ml were labeled as Hypovitaminosis D. After collection of investigations, serum Vitamin D3 levels in PD subjects were determined and proforma filled accordingly.

2.3. Statistical Analysis

The important outcome of study was assessment of vitamin D levels in subjects of PD. All gathered figures analyzed by Statistical Package for Social Science (SPSS) software, edition 20.0. Frequency & percentages computed for categorical variables like gender, and Vitamin D levels. Mean and standard deviation considered for variables (quantitative) as age and vitamin D3 levels. Significance of serum Vitamin D was seen with age, gender, duration of PD to see the impact of these on outcomes. P value < 0.05 was considered statistically significant. Variables (Clinical) communicated as mean ± standard deviation (SD) or percentage as suitable. Chi-square test utilized to review distinctions in ratios. Affiliation among serum vitamin D3, PD and its duration were investigated by bivarate correlation analysis by changing for the covariates (age, sex, BMI, smoking, liquor utilize, pesticide history, BMI and vitamin D). The relationships between serum 25(OH)D and length of PD were examined by bivarate correlation investigation.

3. Results

3.1. Analyses of Age and Vitamin D

In recent study there were a total of 243 subjects with PD who were assessed for frequency of vitamin D deficiency. The Mean age of patients was 67.64 with SD ± 6.67 years minimum 56 and maximum 85 years respectively. Mean values of vitamin D3 levels were 27.68 with SD ± 21.72 ng/ml with minimum 08 ng/ml and maximum values 85.50 ng/ml.

3.2. Analyses of Demographic Data

Most participants were males 170 (70%) and 73 (30%) females, 232 (95.5%) married and 11 (4.5%) were unmarried (p = 0.000). A large number of subjects 162 (66.7%) were from rural and 81(33.3%) from urban community (p = 0.000). By occupation 27 (11.1%) have no any occupation, 73 (30%) house-wives, 100 (41.2%) manual workers and 43 (17.7%) were office workers (p = 0.000). Regarding educational status 64 (26.3%) uneducated, 123 (50.6%) primary to matriculation, 48 (19.8%) intermediate to graduation and only 08 (3.3%) were postgraduates (p = 0.000). A large number of study subjects 213 (87.7%) had no any evidence of PD in family, where as positive family history was observed in 30 (12.3%) subjects (p = 0.000). Evaluating risk factors for PD, history of pesticide contact in 09 (3.7%), smoking 61 (25.1%), alcohol abuse 24 (9.9%) and history of head injury observed in 18 (7.4%) subjects (p = 0.000). BMI normal in 143 (58.8%), over weight in 91 (37.4%) and 09 (3.7%) were obese subjects (p = 0.000). Baseline characteristics of participants as tremors, bradykinesia, speech changes, impaired posture and balance, rigidity and writing changes were observed in 67.1%, 10.7%, 6.2%, 5.8%, 5.3% and 4.9% respectively (p = 0.000). Regarding duration of PD 82 (33.7%) were <01 year, 40 (16.5%) 1 - 2 years, 41 (16.9%) 2 - 5 years, 40 (16.5%) 5 - 10 years and 40 (16.5%) had duration > 10 years (p = 0.000). We identified 151 (62.1%) subjects with vitamin 25(OH)D < 30 ng/ml, remaining 92 (37.9%) have normal vitamin D3 values (30 - 150 ng/ml) (p = 0.000). Insufficiency (10 - 30 ng/ml) found in 148 (60.9%) and deficiency (<10 ng/ml) was seen in 03 (1.2%) subjects (p = 0.000). Rest of chi-square values and df were shown in Table 1.

3.3. Analyses of Different Correlations

The correlation of different variables assessed as shown in Table 2. We found that vitamin D3 levels (p = 0.000) were strongly correlated with age (p = 0.000), duration of PD (p = 0.000) these were statistically significant, and the analysis of other risk factors of PD were also assessed there was not significant correlation of various risk factors of PD and vitamin D deficiency like head injury (p = 0.017) alcohol (p = 0.358), smoking (p = 0.566), pesticide contact (p = 0.512), family history (p = 0.840) and BMI (p = 0.572) as shown in Table 2. The p-value of less than 0.05 was considered statistically significant.

4. Discussion

Pakistan is underdeveloped country with poor control on population growth and lack of resources. There is lot of hindrances in the health management parameters. Here we had carried out a research on PD and vitamin D3 level. PD is disease of old age. Sun exposure is easily available and prevalent throughout the country except few areas. There is poor concept of sunbath. Our male population remains outdoors most of daytime for earning purpose. Burka/Parda is common hindrances of females for sun exposure. Head injury, pesticide exposure,

Table 1. Frequency, percentage and chi-square values of study variables.

Variable	Variables details	Frequency	Percent	Chi-Square	df	Asymp. Sig.
Variable	Total	243	100.0	Non-parametric		
Gender	Male	170	70.0	38.720[b]	1	0.000
	Female	73	30.0			
Marital status	Married	232	95.5	200.992[b]	1	0.000
	Unmarried	11	4.5			
Address	Rural	162	66.7	27.000[b]	1	0.000
	Urban	81	33.3			
Occupation	No Occupation	27	11.1	51.765[c]	3	0.000
	House Wife	73	30.0			
	Manual Workers	100	41.2			
	Office Workers	43	17.7			
Education	Uneducated	64	26.3	112.440[c]	3	0.000
	Primary To Matric	123	50.6			
	Intermediate to Graduate	48	19.8			
	Post Graduate	8	3.3			
Family Hx	Negative Family History PD	213	87.7	137.815[a]	1	0.000
	Positive Family History PD	30	12.3			
Pesticide contact Hx	Pesticide Contact Hx Yes	9	3.7	208.333[b]	1	0.000
	Pesticide Contact Hx No	234	96.3			
Smoking Hx	Smoking Yes	61	25.1	60.251[b]	1	0.000
	Smoking No	182	74.9			
Alcohol Hx	Alcohol History No	219	90.1	136.585	50	0.000
	Alcohol History Yes	24	9.9			
Head injury Hx	Head Injury Yes	18	7.4	176.333[b]	1	0.000
	Head Injury No	225	92.6			
PD symptoms	Tremor	163	67.1	447.840[e]	5	0.000
	Bradykinesia	26	10.7			
	Speech Changes	15	6.2			
	Impaired Posture & Balance	14	5.8			
	Rigidity	13	5.3			
	Writing Changes & Others	12	4.9			
Vit D	Deficiency: 0 - 10 ng/ml	3	1.2	209.704[c]	2	0.000
	Insufficiency: 10 - 30 ng/ml	148	60.9			
	Sufficiency: 30 - 150 ng/ml	92	37.9			
Duration of PD (Years)	<1	82	33.7	132.025[d]	4	0.000
	>1 - 2	40	16.5			

Continued

Vit D Level	>2 - 5	41	16.9	14.325[b]	1	0.000
	>5 - 10	40	16.5			
	>10	40	16.5			
	Normal	92	37.9			
	Hypovitaminosis D	151	62.1			
BMI	Normal	143	58.8	112.691[a]	2	0.000
	Over Weight	91	37.4			
	Obese	9	3.7			

Table 2. Correlation of different variables in Parkinson's disease subjects. Correlations of low levels of Vitamin D levels with other variables of study.

		Level of vitamin D	Duration of PD	Age in years	Hx of head injury	Hx of alcohol intake	Cigarette smoking	Pesticide contact Hx	Family history	BMI
Level of vitamin D	Pearson Correlation	1	−0.649**	−0.656**	0.153*	−0.059	−0.037	−0.042	0.013	0.036
	Sig. (2-tailed)		0.000	0.000	0.017	0.358	0.566	0.512	0.840	0.572
Duration of Parkinson's disease	Pearson Correlation	−0.649**	1	0.814**	−0.129*	0.021	−0.077	0.130*	−0.014	0.013
	Sig. (2-tailed)	0.000		0.000	0.045	0.742	0.232	0.043	0.832	0.840
Age in years	Pearson Correlation	−0.656**	0.814**	1	−0.065	−0.030	−0.198**	0.019	−0.098	0.004
	Sig. (2-tailed)	0.000	0.000		0.314	0.646	0.002	0.771	0.128	0.953
History of head injury	Pearson Correlation	0.153*	−0.129*	−0.065	1	−0.064	−0.164*	−0.055	−0.180**	0.002
	Sig. (2-tailed)	0.017	0.045	0.314		0.318	0.011	0.389	0.005	0.975
History of alcohol intake	Pearson Correlation	−0.059	0.021	−0.030	−0.064	1	0.001	0.065	0.882**	0.030
	Sig. (2-tailed)	0.358	0.742	0.646	0.318		0.990	0.314	0.000	0.641
Cigarette smoking	Pearson Correlation	−0.037	−0.077	−0.198**	−0.164*	0.001	1	−0.114	0.044	0.006
	Sig. (2-tailed)	0.566	0.232	0.002	0.011	0.990		0.077	0.493	0.925
Pesticide contact hx	Pearson Correlation	−0.042	0.130*	0.019	−0.055	0.065	−0.114	1	0.074	0.001
	Sig. (2-tailed)	0.512	0.043	0.771	0.389	0.314	0.077		0.253	0.982
Family history	Pearson Correlation	0.013	−0.014	−0.098	−0.180**	0.882**	0.044	0.074	1	0.078
	Sig. (2-tailed)	0.840	0.832	0.128	0.005	0.000	0.493	0.253		0.225
Body Mass Index	Pearson Correlation	0.036	0.013	0.004	0.002	0.030	0.006	0.001	0.078	1
	Sig. (2-tailed)	0.572	0.840	0.953	0.975	0.641	0.925	0.982	0.225	
	N	243	243	243	243	243	243	243	243	243

*Significant Correlation at 0.05 levels (2-tailed). **Significant Correlation at 0.01 levels (2-tailed).

smoking are common in comparison to alcoholism and obesity in PD. Due to lack of health education, most of time peoples ignore health issues. Currentlyan established role of vitamin D and PD was identified. We carried out a study in our population to check the presence of low levels of vitamin D3 in PD. There is

described role of vitamin D3 lack in PD, vitamin D3 insufficiency leads or progresses to Parkinson's disease. These issues were focused in different studies in rest of world. Findings of present study are match-able with previous studies as discussed below.

PD (Parkinson's disease) is a neurodegenerative disease in a particular zone of the cerebrum called substantia nigra, [19] characterized by inflexible nature, tremors and dyskinesia along with postural insecurity and dementia. Vitamin D had critical effect on neurological illnesses as PD and Dementia. In cerebrum, hippocampus and substantia nigra neurons show high convergences of VDRs in their core and 1-OHase in their cytosol. In present study mean ± SD values of age were 67.64 ± 6.67 years (age range 56 - 85 years), males 170 (70%) and 73 (30%) were females, our findings are supported in a study by Moghaddasi M *et al.* in which mean age of the patients were 56.57 ± 11.71 years (age range 24 - 79 years); 3 (75.9%) males and 20 (24.1%) were females. Mean age of symptoms onset was 50.71 ± 12.10 years (range 20 - 77 years) [20]. With insufficiency of vitamin D, there is hazard of developing PD; this hazard increases to twofold when there is deficiency of vitamin D [21]. Vitamin D levels were low in subjects with PD and AD in comparison to the normal controls, [8] current study also determined insufficiency of vitamin D3 in 61.1% of PD subjects. 25(OH)D3 emphatically connected with intellectual execution, especially with measuring its role in elderly populace [22]. Many of studies (Cross Sectional) had shown the relationship of decreased levels of vitamin D with incident of PD also predicted increased hazard of PD [23]. Vitamin D levels in high-risk group and matched controls (age, sex) did not differ, and it was suggested that there is no deficiency of vitamin D before diagnosis of PD [24]. A majority of researches in established PD had shown lower vitamin D values as compared to fit controls [9]. Serum values of vitamin D decrease as severity of disease increases [25] [26] as low levels of vitamin D3 were observed in subjects of PD in this study.

Nitric Oxide (free radical) can damage to cells, its synthesis is inhibited by vitamin D, and vitamin D3 also causes formation of glutathione (antioxidant) thus plays a neuro-protective role [27]. It is assumed that vitamin D3 is involved in initiating the synthesis of N G F (nerve growth factor), Glial cell line derived factor and NT3 (Neurotrophin) and in this way is considered as Neurotrophic Factor [28] [29] [30]. Peterson *et al.* in their research found strong relationship of automatic postural responses with serum vitamin D concentrations [31]. Daily vitamin D3 supplements (1200 IU) for one year showed mild progression of disease and worsening of disease observed in those who did not receive increments. [32] As there were presence of more than one symptom of PD, VDD was more common as age of patient increases with more than one symptom. Patients with PD had limited outdoor activities so solar exposure is decreased this may contributes to decreasing levels of vitamin D even with incremental intake [33].

Juan Wang *et al.* showed statistically a significant link among vitamin D values and sun exposure; and no involvement among serum vitamin D and daily

oral supplements of vitamin D. There study indicated that low values of this vitamin with reduced sun exposure are associated with increase hazard of PD [34], above associations of VDD and PD are evident in present study. Yoon JH *et al.* in their study subjects with early PD, observed the relation among serum vitamin D values and endothelial cell dysfunction [35]. Probable racial variations in passageway for consumed vitamin D may be dilemma crossways to panel suggestions meant for D3 values as in Inuit. Decreased synthesis of this vitamin is balanced in Inuit through transforming lot of vitamin-D towards its chiefly active type [36]. A Toronto research on Canadians (young) from various origins had average vitamin D3 values that were fundamentally elevated from authorized proposals [37]. 22% European, 78% and 77% of Asian (East, South) heritage had vitamin D3 level < 40 nmol/l (15 ng/ml), compared with previous studies. Toronto study in Asians (East) observed decreased vitamin D3 in contrast with White community [38].

Rural men around Delhi had average 44 nmol/L of D3, in current study 162 (66.7%) subjects from rural and 81 (33.3%) were urban (p = 0.000), with mean vitamin D3 levels 27.68 ± 21.72 ng/ml, these findings are matching with results of study by Rajasree S *et al.* Normal Indians have decreased vitamin D3, not much unusual than Canadian Asians (South). South Indians with IHD had tremendously increased (>222.5 nmol/l) D3 values [39]. In present study with references to above studies we found that 151 (62.1%) subjects have vitamin D3 <30 ng/ml and remaining 92 (37.9%) have sufficient D3 values (30 - 150 ng/ml) (p value 0.000). Insufficiency (10 - 30 ng/ml) in 148 (60.9%) and deficiency (<10 ng/ml) observed in 03 (1.2%) subjects (p = 0.000). Melanin substance demonstrated opposite association with serum 25(OH)D [37]. Uniformly deficient 25(OH)D values seen in Indians (living in India and China). Noteworthy Hereditary minority of French Canadians didn't buildup consumed vitamin D3. Vitamin D3 protein binding polymorphisms had a significant part of variety in serum D3 as totaled intake of vitamin D3 [40] [41]. Different methods controlling metabolism with limited extent of vitamin D values in which vascular capacity is streamlined were associated with increased mortality [42], abnormal functioning and premature aging [43].

Worldwide prevalence of vitamin D deficiency/insufficiency accounts for 1 billion people [13] where south Asians are uniformly affected despite abundant sunshine [44]. Pakistan a rising nation of Asia (South) with an area spreading over scope 24˚35' North and longitude 61˚ East to 78˚ East, seriously facing D3 insufficiency in pregnant ladies, neonates, babies, youngsters, teenagers, grown-ups, and elderly individuals regardless of plentiful daylight [45]. 70% fit volunteers in Pakistan, 84% pregnant ladies in India are distressed by VDD. Sri Lanka and Bangladesh are no exception where 26% boys and 8% girls are victims of VDD [46]. A study demonstrated 66.32% of PD and 22.62% of healthy individuals had mild to moderate VDD (cutoff value < 30 ng/ml). Pakistani population in general had VDD and vitamin D supplementation assumed to be added after clinical

evaluation of population groups [47]. Mansoor *et al.* elucidated that 56.9% men and 43.1% normal women had Vitamin D3 < 20 ng/ml [48]. Sheikh *et al.* observed in 84.3% of tested healthy subjects (38 - 55 years) in Karachi had 25(OH)D levels < 30 ng/ml suggesting extensive VDD prevalence throughout Pakistan declaring Pakistani population a vitamin D deficient [49].

Findings of above studies were considerably in contest with present study where we identified 151 (62.1%) subjects have vitamin D3 < 30 ng/ml. A narrowed danger of death in old age observed with high Vitamin D3 levels while others didn't benefit [50]. Taking supplements are valuable or not still unclear [51]. Increased danger of vitamin D deficiency observed in Blacks comparison to White populace [52]. Further studies needed to find out reasons for these differences and clarify probable part of vitamin D in pathogenesis and clinical path of PD.

5. Conclusion

Vitamin D deficiency is commonly associated in patients suffering from Parkinson's disease. As concluded in present research that as the age advances, risk of Parkinson's disease increases with simultaneous decrease in vitamin D level. As concluded in our study, 62.1% subjects of Parkinson's disease were vitamin D deficient.

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