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Original Research

# A study evaluating the effect of vitamin D and PUFA supplementation coupled with acupuncture therapy on the prognosis of post-stroke fatigue: A comparative study

**[1]Sujatha Puri, [2]Ashwini Telange,**

**[3]Jeenal Singh and [3*]Ravinder Sahu**

[1]Department of Emergency Medicine, [2]Department of Cardiology,
Veer Surendra Sai Institute of Medical Sciences and Research At/Po- Burla,
Dist-Sambalpur, Odisha, India
[3]Department of Pharmacology, Institute of Medical Sciences & SUM Hospital (IMS and SH),
Medical College and Hospital of Siksha 'O' Anusandhan, Bhubaneswar, Odisha

**Article Info**

Correspondence:
Department of Pharmacology, Institute of Medical Sciences & SUM Hospital (IMS and SH), Medical College and Hospital of Siksha 'O' Anusandhan, Bhubaneswar, Odisha

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*rsahuimssum18@gmail.com

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**Abstract**

The present study was done to evaluate the impact of vitamin D, PUFA supplementation and acupuncture therapy on the prognosis of PSF in stroke patients hospitalized to the Institute of Medical Sciences & SUM Hospital (IMS and SH), Medical College and Hospital of Siksha 'O' Anusandhan, Bhubaneswar, between August 2016 and May 2018. After the final follow-up of the group that received PUFA, Vitamin Supplements, and acupuncture therapy The patients had HDL cholesterol1.69 ± 2.0 mmol/L at pre-treatment, which was 3.62 ± 1.6 mmol/L, total cholesterol level 5.9 ± 2.2mmol/L at pre-treatment, which was 5.02± 1.2 mmol/L, LDL cholesterol level 3.9 ± 2.0 mmol/L at pre-treatment, which was 3.0 ± 0.6 mmol/L, normal fasting blood glucose concentration 6.9 ± 1.5mmol/L at pre-treatment, which was 5.9± 1.0 mmol/L, FSS 6.8(4.6-9) at pre-treatment, which was 2.0 and 25-(OH)-D level 14.6± 3.0 ng/ml_at pre-treatment, which was 29.9± 4.0 ng/ml.

Vitamin D, PUFA supplementation could improve fatigue symptoms and outcomes in PSF patients. We suggest that acupuncture might be an effective and safe adjuvant therapy for PSF. The methodological quality of the evidence in this study is inadequate, and it is further limited by the number of trials included and the small sample size, which may result in inaccurate research findings. Therefore, high-quality research are still needed to confirm the benefits of Vitamin D, PUFA and acupuncture for PSF.

**Keywords:** Vitamin D, PUFA, acupuncture, Post-stroke Fatigue and Prognosis

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## Introduction

A stroke can cause significant damage not only to the brain but also to other organs, which may increase the body's need for essential vitamins and minerals to support the healing process. Ensuring an adequate intake of vitamins is therefore crucial for recovery. Many vitamins contain antioxidants that help shield the body from oxidative stress — a key factor that worsens stroke-related injury. By reducing oxidative stress, antioxidants can help lower inflammation, which plays an important role in the recovery phase. Additionally, vitamins strengthen the immune system, which is vital during stroke rehabilitation, as a robust immune response helps fight off infections and complications that may arise during recovery.

However, there is limited clinical evidence to confirm whether supplementing with vitamin D has a clear positive effect on stroke outcomes [1,2]. One of the most common and troublesome complications following a stroke is post-stroke fatigue (PSF), which is marked by a persistent feeling of exhaustion and low energy that does not improve with rest [3]. Early detection and management of fatigue could be key to improving recovery, although the exact biological mechanisms behind PSF remain poorly understood. It is thought to result from a combination of biological, psychological, and behavioral factors [4]. At present, there is insufficient evidence to demonstrate that drug-based treatments for PSF are effective, and overall, medication outcomes remain unsatisfactory [5–7].

Consequently, there is growing interest in exploring non-drug interventions [8]. Acupuncture, one of the oldest forms of non-pharmacological therapy, involves inserting fine needles into specific points on the body at precise angles to address various health conditions [9]. In China, acupuncture has long been used to manage stroke and its related symptoms and is gradually gaining broader global acceptance [10,11]. The World Health Organization (WHO) even endorses acupuncture as a complementary and alternative option for stroke management [12].

The estimated prevalence of PSF ranges widely, affecting about 23% to 75% of stroke survivors, and its symptoms can persist for a year or more [13–15]. PSF is often described as abnormal, persistent fatigue that does not correspond to the level of physical or mental activity performed during recovery. Beyond its impact on daily functioning and emotional well-being, PSF has also been associated with increased mortality rates among stroke patients [16].

Vitamins, as essential micronutrients, play critical roles in maintaining good health by supporting numerous biochemical pathways, including energy metabolism, immune defense, and tissue repair. In the context of stroke rehabilitation, certain vitamins are particularly important. B vitamins, for instance, are vital for the proper functioning of the nervous system and cognitive processes. Vitamin B6 (pyridoxine) is involved in the synthesis of neurotransmitters such as serotonin, dopamine, and gamma-aminobutyric acid (GABA). This vitamin can help enhance mental clarity, prevent apathy, and improve sleep quality [17]. Moreover, vitamins B6 and B12 serve as coenzymes in the methylation of homocysteine, an amino acid that, when elevated, can accelerate atherosclerosis and raise the risk of stroke.

## Study design and populations

The present study was done to evaluate the impact of vitamin D, PUFA supplementation and acupuncture therapy on the prognosis of PSF in stroke patients hospitalized to the Institute of Medical Sciences & SUM Hospital (IMS and SH), Medical College and Hospital of Siksha 'O' Anusandhan, Bhubaneswar, between August 2016 and May 2018. This specific version of the questionnaire was organized assess the impact of Vitamin D and PUFA Supplementation and acupuncture on post stroke patients.

The demographic and clinical characteristics at baseline were collected (Table 1), A total of 47 participants was included in the study to test the questionnaire. We received a written

consent form from each participant. Also, the study approval was obtained by the ethics committee of Institute of Medical Sciences & SUM Hospital (IMS and SH), Medical College and Hospital of Siksha 'O' Anusandhan, Bhubaneswar, In the current study, a total of 47 patients with breast cancer referring to the Hospital, were selected and divided into 2 groups (Participants n=47 and control group n=12).

**Inclusion and Exclusion Criteria**

Inclusion criteria were the following: age 30 - 65 years; The time period of stroke within the last 2 years was chosen because the level of post-stroke fatigue has previously been shown to remain constant for up to 2 years [18]. A sampling strategy was used and aimed to recruit participants with diversity in age, gender, physical impairment and living accommodations. Exclusion criteria includes patients on dialysis, diagnosed with transient ischemic attack, nervous system disease/disorder and inability to provide informed consent

**Ethical standards:**

This study was carried out in accordance with the specific national laws and ethical standards specified in the 1964 Declaration of Helsinki and its amendments. The Institutional Ethics Committee approved the study, and all participants provided informed consent prior to any experimental procedure.

**Data Measurement**

Present study we collected the information on participant demographics, including stroke subtype, current smoking, and arterial blood pressure, hypertension, diabetes, and coronary heart disease (CHD) using a structured questionnaire. The average daily intake was measured by amount and associated nutrient content of food item data collected in terms of (never or rarely, once a week, four times a week, once a day and twice a day) included in the food frequency questionnaire.

Follow-up evaluations were conducted at both four weeks and twelve weeks. The Fatigue Severity Scale (FSS) is a widely used tool for distinguishing between individuals who experience significant fatigue and those who do not. Its psychometric properties have been tested extensively and shown to be valid and reliable across various clinical populations [19,20]. The FSS consists of seven items, with higher average scores indicating greater fatigue severity [21]. For this study, fatigue was defined as having a mean FSS score of 4 or higher [20]. Each item is rated using a seven-point Likert scale, ranging from 1 (“strongly disagree”) to 7 (“strongly agree”), and the mean of all items provides the final score. Some studies alternatively calculate the total FSS score by summing all item responses.

Statistical significance was defined at a p-value threshold of 0.05. All statistical analyses were carried out using SPSS version 18 (IBM Corp., Armonk, NY, USA). Baseline laboratory assessments, including fasting blood glucose, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and total cholesterol (TC), were completed within the first 24 hours after hospital admission.

Vitamin D levels were measured to detect deficiencies that could be corrected through supplementation before leading to further health complications. The most accurate way to evaluate vitamin D status is by measuring serum 25-hydroxyvitamin D [25(OH)D]. Venous blood samples were collected in standard biochemical tubes within 24 hours of admission, and serum 25(OH)D levels were determined using a modern chemiluminescent immunoassay. Vitamin D deficiency was defined as a serum 25(OH)D concentration below 20 ng/ml [22,23]. To examine the relationship between fatigue and vitamin D status, Pearson’s correlation coefficients (r) were calculated between FSS scores and serum 25(OH)D levels.

Regarding acupuncture treatment, the five most frequently used acupoints were Baihui (GV20), Qihai (CV6), Guanyuan (CV4), Zusanli

(ST36), and Sanyinjiao (SP6), with Baihui (GV20) being the most commonly selected point.

Both intervention groups demonstrated similar baseline characteristics in terms of demographic factors such as age and sex, as well as comparable clinical and biochemical measurements. Detailed demographic and clinical information for the participants is presented in Table 1.

**Table1**: Characteristics of the Patients at Baseline.

| Variables | | Participants (n=47) Pre- treatment | % -- | Control Group n=12 | % -- |
|---|---|---|---|---|---|
| **Age** | | 42.9 ± 8.2 | | 48.5 ± 6.9 | |
| **Genetic information (Yes)** | | 6 | | 1 | |
| **Time since stroke, in months** | 2–9 months | 19 | 40.42 | 6 | 50 |
| | 10-19 months | 15 | 31.91 | 5 | 41.66 |
| | 20–24 months | 13 | 27.65 | 1 | 8.33 |
| **Gender** | Male | 36 | 76.59 | 8 | 66.66 |
| | Female | 11 | 23.40 | 4 | 33.33 |
| **Marital status** | Single | 7 | 14.89 | 2 | 16.66 |
| | Married | 38 | 80.85 | 10 | 83.33 |
| | divorced and widowed | 2 | 4.25 | 0 | |
| **Education** | Upto Std 5$^{th}$ | 12 | 25.53 | 2 | 16.66 |
| | Upto Std 10$^{th}$ | 6 | 12.76 | 3 | 25 |
| | Upto 12$^{th}$ | 9 | 19.14 | 5 | 41.66 |
| | Degree/Graduation | 17 | 36.17 | 1 | 8.33 |
| | Post Graduation | 3 | 6.38 | 1 | 8.33 |
| **Residence** | Urban | 26 | 55.13 | 7 | 58.33 |
| | Rural | 21 | 44.68 | 5 | 41.66 |
| **Occupation** | Labour work | 14 | 29.78 | 4 | 33.33 |
| | Office work | 26 | 55.31 | 7 | 58.33 |
| | Unemployed | 7 | 14.89 | 1 | 8.33 |
| **Addicts** | Smoker | 31 | 65.95 | 4 | 33.33 |
| | Alcoholic | 14 | 29.78 | 6 | 50 |
| | No Addicts | 2 | 4.25 | 2 | 16.66 |
| **Stroke subtype** | large artery Therosclerosis | 26 | 55.31 | 7 | 58.33 |
| | small vessel occlusion | 17 | 36.17 | 3 | 25 |
| | Cardioembolism | 4 | 8.51 | 2 | 16.66 |
| **Disability at stroke** | Severe | 27 | 57.44 | 4 | 33.33 |
| | Moderate | 13 | 27.65 | 3 | 25 |

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|---|---|---|---|---|---|
| | Slight | 7 | 14.89 | 1 | 8.33 |
| | No | 0 | | 4 | 33.33 |
| **Hypertension** | Severe | 20 | 42.55 | 6 | 50 |
| | Moderate | 15 | 31.91 | 3 | 25 |
| | Slight | 12 | 25.353 | 3 | 25 |
| | No | 0 | | 0 | |

**Results:**

**Efficacy of Vitamin and PUFA Supplements and Acupuncture Compared to Control**

The effectiveness of combining vitamin supplements, polyunsaturated fatty acid (PUFA) supplements, and acupuncture therapy was compared with a control group, as summarized in Table 2.

Regarding **HDL cholesterol**, it is important to note that not all cholesterol is detrimental to health. High-density lipoprotein (HDL) cholesterol — often called "good" cholesterol — is associated with a lower risk of cardiovascular disease. An HDL level of 60 mg/dL (1.55 mmol/L) or higher is generally considered protective, whereas levels below 40 mg/dL (1.03 mmol/L) are less desirable. In this study, patients in the intervention group had an average HDL cholesterol of $1.69 \pm 2.0$ mmol/L before treatment, which increased to $3.62 \pm 1.6$ mmol/L after 12 weeks of PUFA, vitamin, and acupuncture treatment. By comparison, the control group recorded an HDL cholesterol level of $2.3 \pm 1.0$ mmol/L at the final follow-up, with no statistically significant difference ($p > 0.05$).

**Fatigue Severity Scale (FSS)** scores differed notably between groups. At 12 weeks, the treatment group showed a significantly greater reduction in fatigue compared to controls, suggesting that the combined intervention could be a promising approach for managing fatigue symptoms.

In terms of **total cholesterol**, a level below 200 mg/dL (5.17 mmol/L) is considered normal; 200–239 mg/dL (5.17–6.18 mmol/L) is borderline high; and 240 mg/dL (6.21 mmol/L) or higher is classified as high. In the intervention group, mean total cholesterol was $5.9 \pm 2.2$ mmol/L before treatment and declined to $5.02 \pm 1.2$ mmol/L after 12 weeks. The control group's total cholesterol at follow-up was $5.1 \pm 1.8$ mmol/L.

For **LDL cholesterol**, levels below 2.6 mmol/L (100 mg/dL) are optimal; 2.6–3.3 mmol/L (100–129 mg/dL) is above optimal; and 3.4–4.1 mmol/L (130–159 mg/dL) is borderline high. Initially, the intervention group's LDL cholesterol was $3.9 \pm 2.0$ mmol/L, which dropped to $3.0 \pm 0.6$ mmol/L by the end of the study. The control group showed an LDL cholesterol level of $3.3 \pm 2.0$ mmol/L at final follow-up.

**Fasting blood glucose** levels typically range between 70–100 mg/dL (3.9–5.6 mmol/L). Patients in the intervention group had an initial mean fasting glucose of $6.9 \pm 1.5$ mmol/L, which decreased to $5.9 \pm 1.0$ mmol/L after treatment. In the control group, the fasting glucose level was $6.2 \pm 1.0$ mmol/L at follow-up.

For **vitamin D status**, 25-hydroxyvitamin D [25-(OH)-D] levels below 20 ng/ml indicate deficiency, levels between 21–29 ng/ml are considered insufficient, and levels above 30 ng/ml are ideal for optimal health benefits. Research has shown that restoring normal vitamin D levels may help reduce fatigue in various medical conditions [24–26]. In this study, patients receiving PUFA, vitamins, and acupuncture started with an average 25-(OH)-D level of $14.6 \pm 3.0$ ng/ml, which increased to $29.9 \pm 4.0$ ng/ml at follow-up. The control group, meanwhile, had a 25-(OH)-D level of $21.5 \pm 2.6$ ng/ml at the end of the study.

Regarding **fatigue**, measured with the nine-item FSS (where each item is scored from 1 to 7, with higher scores indicating more severe fatigue and greater impact on daily life), the intervention group's mean FSS dropped from 6.8 (range 4.6–9) before treatment to 2.0 at the final follow-up. The control group recorded a mean FSS of 4 (range 3–5) at follow-up.

**Table2:** Efficacy of Vitamin, PUFA supplements and acupuncture versus control group

| Variables | Participants (n=47) Pre- treatment | Follow up 4 week | Follow up 12 week | control group n=12 Pre-treatment | Follow up 4 week | Follow up 12 week |
|---|---|---|---|---|---|---|
| **Fatigue (FSS7)** | 6.8(6-9) | 4.2(3-4) | 2.0(2-3) | 6(2-2.6) | 5(4-6) | 4(3-5) |
| **total cholesterol, mmol/L** | 5.9 ± 2.2 | 5.3± 1.0 | 5.02± 1.2 | 5.7 ± 1.3 | 5.6± 1.5 | 5.1± 1.8 |
| **high-density lipoprotein mmol/L** | 1.69 ± 2.0 | 2.32 ± 1.0 | 3.62 ± 1.6 | 1.9 ± 1.6 | 2.0 ± 1.8 | 2.3 ± 1.0 |
| **low-density lipoprotein, mmol/L** | 3.9 ± 2.0 | 3.6 ± 1.0 | 3.0 ± 0.6 | 3.8 ± 1.6 | 3.7 ± 1.9 | 3.3 ± 2.0 |
| **fasting blood glucose, mmol/L** | 6.9 ± 1.5 | 6.4± 1.2 | 5.9± 1.0 | 6.7 ± 1.9 | 6.6± 1.5 | 6.2± 1.0 |
| **25-(OH)-D, ng/ml** | 14.6± 3.0 | 18.9± 3.6 | 29.9± 4.0 | 15.0± 2.1 | 16.2± 2.6 | 21.5± 2.6 |

**Discussion**

This study is the first to comprehensively and dynamically examine the combined impact of vitamin D, polyunsaturated fatty acid (PUFA) supplementation, and acupuncture on post-stroke fatigue and related outcomes. After 12 weeks of vitamin D supplementation, the intervention group demonstrated significantly lower fatigue levels compared to the control group. Vitamin D, a fat-soluble steroid hormone, plays a key role in maintaining calcium balance. In addition, it contributes to cell growth, modulates immune responses, and regulates various endocrine pathways [27]. The body primarily produces vitamin D through sunlight exposure, while dietary sources include fish, fortified dairy products, and eggs [28].

Growing evidence indicates that low vitamin D levels are linked to greater stroke severity, larger infarct sizes, and higher mortality rates following a stroke [29–31]. Similarly, a diet lacking in omega-3 PUFAs has been shown to cause synaptic impairment and adverse neuronal changes [32]. Another omega-3 PUFA, eicosapentaenoic acid (EPA 20:5(n-3)), has been found to interact with both the immune and endocannabinoid systems, thereby supporting neuronal repair and brain recovery [33]. In this study, fatigue severity scores (FSS) were significantly different between the groups, with the intervention group reporting notably improved fatigue outcomes at 12 weeks. These results suggest that this combined approach may offer a practical strategy for alleviating post-stroke fatigue. Taken together, our findings indicate that vitamin D supplementation may help reduce fatigue symptoms and improve overall recovery in patients with post-stroke fatigue.

Acupuncture, which has been used for centuries in China to manage stroke and its complications, remains popular due to its consistent effectiveness, simplicity, and safety profile [34]. Although the exact mechanisms underlying post-stroke fatigue are still not fully understood and are thought to involve complex biological and psychological factors [38], acupuncture may help relieve stroke-related symptoms by promoting neural regeneration, reducing inflammation, improving cerebral circulation, and mitigating oxidative stress [34–37].

The five most commonly used acupoints in this study were Baihui (GV20), Qihai (CV6), Guanyuan (CV4), Zusanli (ST36), and

Sanyinjiao (SP6). According to the principles of traditional Chinese medicine (TCM), these points are believed to replenish Qi, invigorate blood flow, regulate vital energy, and stimulate brain function [39]. The therapeutic effects of these acupoints may therefore help reduce fatigue symptoms in stroke patients.

Overall, these findings highlight the potential value of integrating vitamin supplementation, PUFA intake, and acupuncture therapy as a combined approach to managing fatigue in stroke survivors.

**Conclusion**

Vitamin D and PUFA supplementation appear to help alleviate fatigue symptoms and improve outcomes in individuals with post-stroke fatigue (PSF). Compared to standard care alone, combining acupuncture with conventional treatment has shown promising potential for reducing fatigue severity as measured by the FSS. These findings suggest that acupuncture could serve as an effective and safe complementary therapy for managing PSF. However, the methodological quality of the current evidence is limited, partly due to the small number of studies included and the relatively modest sample size, which could affect the reliability of the results. Consequently, larger, well-designed, high-quality studies are necessary to confirm the potential benefits of vitamin D, PUFA supplementation, and acupuncture for PSF patients.

**Data Availability Statement**

The original contributions presented in the study are included in the article; further inquiries can be directed to the corresponding author/s.

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**Declarations**

**Ethics approval and consent to participate**

The study was approved by the Institute of Medical Sciences & SUM Hospital (IMS and SH), Medical College and Hospital of Siksha 'O' Anusandhan, Bhubaneswar, Odisha, India. All participants received written information about the study, gave written consent and were informed about their ability to withdraw from the study at any time before publication of results.

**Competing interests**

The authors declare that there are no conflicts of interest.

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