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Research Article

IMPACT OF PHYSICAL THERAPY APPROACH IN SUBJECTS WITH POST-DENGUE FATIGUE SYNDROME

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ABSTRACT

Objectives: The objective of the study was to study the effectiveness of an innovative exercise regimen in alleviating fatigue and enhancing health-related quality-of-life (HRQoL) in individuals suffering from post-dengue fatigue syndrome (PDFS).

Methods: A randomized controlled trial was conducted, with participants diagnosed with PDFS. The innovative exercise protocol included aerobic exercises, graded exercises, breathing exercises, emotional liberation-breathing, Jacobson exercises, and psycho-neurobics, administered over a 6-week period. Both groups received face-to-face and online interaction and video calls for guidance. The outcome measures were the fatigue severity scale (FSS) and HRQoL, assessed before and after the intervention.

Results: The 6-week rehabilitation program led to significant improvements in both groups, as reflected by reduced fatigue levels, evaluated using the FSS, and enhanced HRQoL components. Notably, the experimental group exhibited more significant improvements in reducing fatigue and six HRQoL components, although no significant improvements were observed in surface fitting and grasshopper components. The innovative exercise protocol, alongside the home-based exercise regimen, demonstrated statistically significant effects on alleviating fatigue and improving HRQoL in PDFS patients.

Conclusion: This research underscores the potential of exercise interventions in managing PDFS, shedding light on the beneficial impact of innovative exercise routines on fatigue and HRQoL in individuals dealing with PDFS. Nonetheless, tailored approaches may be necessary to target specific components of HRQoL, such as social functioning and general health, warranting further investigation in this domain.

Keywords: Post-dengue fatigue syndrome, Health-related quality-of-life, Physical therapy, Exercise, Chronic fatigue.

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INTRODUCTION

Dengue fever is by the dengue virus (DENV1, DENV2, DENV3, and DENV4). It is a global public health concern prevalent in subtropical and tropical regions. This mosquito-borne arboviral infection is primarily spread by both *Aedes aegypti* and *Aedes albopictus* female mosquitoes, known for their daytime feeding habits [1]. It ranks second only to malaria as a significant vector-borne viral illness, impacting global health with rising incidence and fatality rates [2]. The economic burden and the prevalence of vector-borne diseases, including dengue, have steadily increased from 1990 to 2019, often with underreporting [3].

Approximately 2.5 million individuals are at risk of contracting dengue, with exposure to any of the four DENV strains, and an incubation period of 3–7 days [4]. World Health Organization estimates dengue fever affects approximately 50–100 million people annually, including a substantial number of life-threatening cases, with a 30% increase in incidence over the last 50 years [5].

Dengue fever presents initially with flu-like symptoms, including severe headache, high fever, fatigue, muscle soreness, and skin dermatitis causing itching and irritation, often referred to as "breakbone fever" [6]. Severe cases may lead to elevated blood pressure, nausea, diarrhea, stomach discomfort, or altered cognitive function, resulting in dengue shock [7].

The primary mode of dengue transmission is through the bites of infected female mosquitoes, with *A. aegypti* as the primary vector [8]. Although other *Aedes* species can transmit the virus, their impact is relatively minimal [9]. The virus enters the human system through a mosquito's bite, attaching to white blood cells and beginning replication [10]. The extrinsic incubation period, the time from virus acquisition to transmission to a new host, is influenced by temperature, viral genetics, and viral concentration [11].

Transmission of the virus from humans to mosquitoes can take place, involving individuals who exhibit symptoms, those in a pre-symptomatic state, and even those who are asymptomatic. Once a mosquito feeds on an infected person, the virus undergoes replication in the mosquito's midgut, subsequently migrating to other tissues such as the salivary glands. This process occurs both before the appearance of symptoms and for a period of up to 2 days following the subsiding of fever [12]. The risk of mosquito infection is closely associated with the patient's viremia and fever levels. It has been observed that higher levels of DENV-specific antibodies can effectively reduce the risk of mosquito transmission [13]. While mosquito vectors are the primary means of transmission, there is also evidence of transmission during pregnancy. The rate of vertical transmission during pregnancy is relatively low and depends on the timing of infection during gestation [14].

Approximately 25% of dengue patients experience post-infectious fatigue syndrome (PIFS) following recovery [15]. PIFS includes neurological and muscular symptoms, such as acute-macular neuropathies, neuritis, limb paralysis, severe headaches, myositis, myalgia, hypokalemia paralysis, and muscle weakness, contributing to pain and discomfort, particularly during physical activities.

Myositis, an inflammation of skeletal muscle, results in motor weakness in the limbs and trunk, with the precise etiology unidentified. Muscle

dysfunction is linked to metabolic rate reduction, muscle edema, and endothelial tissue changes [16]. Myalgia, marked by muscle rigidity, swelling, discomfort, and tenderness, is common during the early stages of dengue fever, affecting the lower back, arm, and leg muscles [17,18].

Treatment for dengue typically involves broad-spectrum antiviral pharmacological measures and supportive care, with no specific antiviral agent available [19,20]. Similarly, there is no established treatment strategy for PIFS. The research aims to evaluate chronic fatigue in patients with PDFS, with a focus on improving fatigue levels health-related quality-of-life (HRQoL). Considering the health implications of dengue and its complications, investigating the potential benefits of physical therapy for individuals recovering from this infectious disease is vital.

METHODS

Study design

An investigative study employing a randomized controlled trial was undertaken to evaluate the efficacy of physical therapy in alleviating post-dengue fatigue syndrome (PDFS) among individuals who had previously suffered from dengue fever. This research was carried out at the outpatient department (OPD) within the Department of Physiotherapy, situated at Lovely Professional University in Phagwara, India. The study duration spanned from September 2022 to February 2023. Before participation in the study, all subjects provided their informed consent in writing, reaffirming the ethical and procedural integrity of the research.

Study population

About 61 individuals were selected from the OPD and the Department of Physiotherapy, both located within the campus of Lovely Professional University in Phagwara, situated in the state of Punjab. The inclusion criteria were both males and females aged between 20 and 60 years and scoring above 32 in the fatigue severity scale (FSS). Exclusion criteria were those with cardiac, renal, and neurological complications, those who were already on physiotherapy rehabilitation for dengue, and those who did not give consent to participate in this study.

Research quality and ethics statement

This study was approved by the Institutional Ethics Committee at the Department of Physiotherapy, situated at Lovely Professional University in Phagwara, India. (Approval # LPU/IEC/2022/01/19) and the study protocol was duly registered with the clinical trials registry under the registration code CTRI/2022/09/046062. The authors followed the applicable EQUATOR Network (http://www.equator-network.org/) guidelines, specifically the STROBE guideline, during the conduct of this research project.

Sampling method

The sampling procedure involved a random selection method employing a lottery approach. Utilizing a simple random sampling technique, the participants were categorically divided into two distinct groups: Group A, designated as the experimental cohort, and Group B, identified as the control group.

Sample size

To determine the required sample size, we employed the G Power software, resulting in a total calculated sample size of 50, factoring in a 15% allowance for potential dropouts. The determination of this sample size took into account statistical power at 80%, an effect size of 0.4, and an alpha level of 0.05. This rigorous approach ensures the statistical validity and reliability of the study's findings.

Study tools

Within this investigation, we utilized two pivotal instruments for evaluation: The FSS and the HRQoL questionnaire, specifically the SF-36. The FSS serves as a self-reported scale, comprising nine items designed to measure the severity of fatigue and its implications on daily life. Scores on the FSS span from one to seven, with higher values indicative of more pronounced fatigue. The completion of this questionnaire typically requires about 8 min.

The assessment of HRQoL was carried out employing the SF-36, a comprehensive questionnaire featuring 36 items that encompass eight distinct facets of HRQoL. These facets include physical functioning (PF), social interaction, and mental well-being. Each item within the SF-36 is rated on a scale ranging from 0 (representing the poorest health status) to 100 (indicating the optimal health state. This comprehensive approach enables a thorough evaluation of participants' HRQoL.

Study procedure

The study's procedure involved the random allocation of participants. Experimental group engaged in a 6-week rehabilitation program with five sessions per week. These sessions took place both in person, at a hospital and a university physiotherapy OPD, and through video calls and social media interactions. The control group, on the other hand, followed a home-based exercise protocol. The interventions encompassed a range of approaches, including graded exercise therapy (GET) to enhance functional ability, aerobic exercises to boost cardiovascular capacity, breathing exercises to improve oxygen-carrying capacity and reduce stress, Jacobson relaxation exercises to promote mental well-being and reduce stress, emotional liberation breathing for eliminating negative emotions, and psycho-neurobics, a meditation-based exercise to enhance mental health.

For Group B, the home-based exercise protocol involved a structured regimen. It began with a warm-up, including a 5–7-min walk that gradually increased in duration. Participants performed flexibility exercises for the upper and lower limbs (3–5 reps daily) and breathing exercises. Initially, they focused on diaphragmatic breathing, and from the 3rd week onward, they transitioned to nose-to-mouth breathing, with repetitions gradually increasing over time. These interventions collectively aimed to address PDFS and enhance the well-being and quality of life of individuals recovering from this condition.

Follow-up

An assessment of the patients' fatigue levels was conducted at the conclusion of the 6th week, employing the same standardized questionnaire for outcome measurement.

Data analysis

The data underwent analysis through IBM Statistical Packages for the Social Sciences version 21. For qualitative variables, descriptive statistics were computed, presenting results as counts and percentages, while for quantitative variables, the means and standard deviations were determined. Intra-group distinctions for both Group A and Group B were assessed using a paired t-test, while interventional and control group disparities were examined through an unpaired t-test. This rigorous statistical approach enabled a comprehensive examination of the data.

RESULTS

A total of 61 participants were initially included in the research, with 11 individuals experiencing attrition, leading to the division of the remaining participants into two groups, each comprising 25 subjects. The demographic characteristics of the study population can be found in Table 1. The experimental group exhibited a mean age of 29.61 years (with a standard deviation of 6.01), while the control group had a slightly lower mean age of 28.61 years (with a standard deviation of 8.36). In terms of weight, the experimental group had a mean weight of 71.50 kg (with a standard deviation of 10.11), whereas the control group had a slightly lower mean weight of 69.88 kg (with a standard deviation of 12.44). Regarding height, the experimental group had a mean height of 167.50 cm (with a standard deviation of 3.81), and the control group had a slightly lower mean height of 164.89 cm (with a standard deviation of 4.92). The body mass index (BMI) was also comparable, with the experimental group having a mean BMI of 25.48 kg/m^2 (with a standard deviation of 3.57) and the control group having a mean BMI of 25.66 kg/m^2 (with a standard deviation of 4.16).

In Group A, there were 11 males (constituting 44% of the group) and 14 females (making up 56% of the group). Group B had 13 males (comprising 52% of the group) and 12 females (constituting 48% of the group). Significant findings within Group A are summarized in Table 2, highlighting enhancements in various domains of HRQoL following the intervention. These improvements include increased scores in PF (Pre-PH to Post-PH), role of limitation in physical health (Pre-RL-PH to Post-RL-PH), role of limitation in emotional health (Pre-RL-EH to Post-RL-EH), energy (Pre-energy to Post-energy), emotional well-being (Pre-EWB to Post-EWB), body pain (Pre-PAIN to Post-PAIN), social life (Pre-SF to Post-SF), and general health (Pre-GH to Post-GH). In addition, a substantial decrease in the FSS score (Pre-FSS to Post-FSS) signifies a positive outcome in fatigue management within the experimental group.

Table 3 outlines significant findings within Group A, where paired differences were scrutinized. Notable results include significant enhancements in PF (Pre-post [PF]), RL-PF (Pre-post [RL-PH]), emotional well-being (Pre-post [EWB]), body pain (Pre-post [PAIN]), energy (Pre-post [ENERGY]), social life (Pre-post [SF]), general health (Pre-post [GH]), and a reduction in the FSS scores (Pre-post [FSS]).

These outcomes are characterized by low $p<0.001$, signifying statistically significant improvements in these domains, underscoring the positive impact of the intervention on fatigue and HRQoL within Group A.

In Group B, the paired differences between pre- and post-intervention assessments reveal noteworthy improvements in several key domains (Table 4).

Table 1: Demographic characteristics among the study population

Demographic variables	Experimental group		Control group	
	Mean	Standard deviation	Mean	Standard deviation
Age (years)	29.61	6.01	28.61	8.36
Weight (kg)	71.50	10.11	69.88	12.44
Height (cm)	167.50	3.81	164.89	4.92
BMI (kg/m^2)	25.48	3.57	25.66	4.16

BMI: Body mass index

Table 2: Comparisons of paired mean and standard deviation of FSS and HRQoL within Group A

Variables	Mean	SD	SE
Pre-PH	50.27	13.66	03.22
Post-PH	61.38	10.11	02.38
Pre-RL-PH	39.44	15.51	03.65
Post-RL-PH	70.00	12.24	02.88
Pre-RL-EH	51.81	73.40	17.30
Post-RL-EH	57.92	23.79	05.60
Pre-energy	43.11	07.90	01.86
Post-energy	58.70	10.79	02.54
Pre-EWB	48.88	11.44	02.69
Post-EWB	65.77	11.28	02.65
Pre-pain	47.95	16.65	03.92
Post-pain	66.97	12.83	03.02
Pre-SF	42.04	10.22	02.40
Post-SF	62.26	12.72	02.99
Pre-GH	46.94	11.13	02.62
Post-GH	58.33	07.27	01.71
Pre-FSS	05.67	01.28	00.30
Post-FSS	03.87	01.14	00.26

FSS: Fatigue severity scale, HRQoL: Health-related quality-of-life, PF: Physical functioning, RL-PH: Role of limitation physical health, RL-EH: Role of limitation emotional health, EN: Energy. EWB: Emotional well-being, SF: Social life, BP: Body pain, GH: General health; SD: Standard deviation; SE: Standard error

These improvements are evident in PF (Pre-post [PF]), RL-PF (Pre-post [RL-PH]), energy (Pre-post [energy]), emotional well-being (Pre-post [EWB]), body pain (Pre-post [Pain]), social life (Pre-post [SF]), general health (Pre-post [GH]), and a reduction in the FSS scores (Pre-post [FSS]). These improvements are marked by low $p<0.001$, signifying significant enhancements in these aspects, highlighting the positive impact of the intervention on fatigue and HRQoL within Group B (Table 5).

Notably, a significant improvement was observed between Group A and Group B in terms of FSS and HRQoL. Within the HRQoL outcome measures, eight domains were assessed, out of which six domains exhibited significant improvement (PF, RL-PH, RL-EH, EN, EWB, BP), while two domains (SF, GH) did not demonstrate a significant difference between Group A and Group B (Table 6).

DISCUSSION

This study aimed to explore the effectiveness of a physical therapy intervention for individuals experiencing PDFS [21]. The findings of this research align with existing literature (references 85–87), reinforcing the notion that innovative exercise regimens, including home-based exercises, yield statistically significant improvements in fatigue levels and quality of life for PDFS patients. In Group A, substantial enhancements in

Table 3: Comparisons of FSS and HRQoL in Group A

Outcomes	Paired differences				p-value
	Mean	SD	SE	T	
Pre-post (PF)	11.11	14.30	03.37	−3.29	0.004
Pre-post (RL-PH)	30.55	19.54	04.60	−6.63	0.001
Pre-post (RL-EH)	06.11	71.98	16.96	−0.36	0.723
Pre-post (EWB)	16.88	05.54	01.30	−12.93	0.001
Pre-post (PAIN)	19.02	10.74	02.53	07.51	0.001
Pre-post (ENERGY)	15.59	04.77	01.12	−13.86	0.001
Pre-post (SF)	20.22	08.16	01.92	−10.50	0.001
Pre-post (GH)	11.38	10.11	02.38	−04.77	0.001
Pre-post (FSS)	01.80	00.74	00.17	10.22	0.001

FSS: Fatigue severity scale, HRQoL: Health-related quality-of-life, PF: Physical functioning, RL-PH: Role of limitation physical health, RL-EH: Role of limitation emotional health, EN: Energy. EWB: Emotional well-being, SF: Social life, BP: Body pain, GH: General health; SD: Standard deviation; SE: Standard error

Table 4: Comparisons of paired mean and standard deviation of FSS and HRQoL within Group B

Outcomes	Mean	SD	SE
Pre-PH	44.16	09.27	2.18
Post-PH	54.72	10.21	2.40
Pre-RL-PH	33.88	18.51	4.36
Post-RL-PH	47.22	13.95	3.28
Pre-RL-EH	25.90	24.37	5.74
Post-RL-EH	40.70	21.53	5.07
Pre-energy	42.22	08.26	1.94
Post-energy	53.05	08.93	2.10
Pre-EWB	49.05	08.41	1.98
Post-EWB	54.27	09.13	2.15
Pre-pain	49.37	13.46	3.17
Post-pain	57.68	13.35	3.14
Pre-SF	46.56	12.25	2.88
Post-SF	56.31	12.11	2.85
Pre-GH	48.05	16.00	3.77
Post-GH	56.94	10.99	2.59
Pre-FSS	05.02	01.34	0.31
Post-FSS	06.01	01.21	0.28

FSS: Fatigue severity scale, HRQoL: Health-related quality-of-life, PF: Physical functioning, RL-PH: Role of limitation physical health, RL-EH: Role of limitation emotional health, EN: Energy, EWB: Emotional well-being, SF: Social life, BP: Body pain, GH: General health; SD: Standard deviation; SE: Standard error

Table 5: Comparisons of FSS and HRQoL in Group B

Outcomes	Paired differences				p-value
	Mean	Standard deviation	Std. Error	t	
Pre-post (PF)	10.55	05.39	1.27	−8.30	0.001
Pre-post (RL-PH)	13.33	06.85	1.61	−8.24	0.001
Pre-post (RL-EH)	14.80	20.50	4.83	−3.06	0.007
Pre-post (ENERGY)	10.83	06.69	1.57	−6.86	0.001
Pre-post (EWB)	05.22	08.74	2.06	−2.53	0.021
Pre-post (PAIN)	08.31	04.10	0.96	−8.59	0.001
Pre-post (SF)	09.75	05.82	1.37	−7.10	0.001
Pre-post (GH)	08.88	08.66	2.04	−4.35	0.001
Pre-post (FSS)	00.98	01.15	0.027	−3.63	0.002

FSS: Fatigue severity scale, HRQoL: Health-related quality-of-life, PF: Physical functioning, RL-PH: Role of limitation physical health, RL-EH: Role of limitation emotional health, EN: Energy, EWB: Emotional well-being, SF: Social life, BP: Body pain, GH: General health, SD: Standard deviation, SE: Standard error

Table 6: Comparisons of mean and standard deviation between groups A and B (FSS and HRQoL)

Post-test readings	Mean	SD	SE	p-value
PH				
Group B	54.72	10.21	2.40	0.970
Group A	61.38	10.11	2.38	
RL-PH				
Group B	47.22	13.95	3.28	0.211
Group A	70.00	12.24	2.88	
RL-EH				
Group B	40.70	21.53	5.07	0.682
Group A	57.92	23.79	5.60	
Energy				
Group B	53.05	08.93	2.10	0.481
Group A	58.70	10.79	2.54	
EWB				
Group B	54.27	09.131	2.15	0.350
Group A	65.77	11.28	2.65	
PAIN				
Group B	57.68	13.35	3.14	0.555
Group A	66.97	12.83	3.02	
SF				
Group B	56.31	12.11	2.85	0.878
Group A	62.26	12.72	2.99	
GH				
Group B	56.94	10.99	2.59	0.079
Group A	58.33	07.276	1.71	
FSS				
Group B	6.01	01.213	0.28	0.947
Group A	3.87	01.145	0.26	

FSS: Fatigue severity scale, HRQoL: Health-related quality-of-life, PF: Physical functioning, RL-PH: Role of limitation physical health, RL-EH: Role of limitation emotional health, EN: Energy. EWB: Emotional well-being, SF: Social life, BP: Body pain, GH: General health, SD: Standard deviation, SE: standard error

fatigue levels and HRQoL components were observed as a result of GET, respiratory exercises, and aerobic workouts [22]. These improvements were particularly evident in the FSS and HRQoL domains, such as PF and RL-PF [23]. The study recognizes the impact of environmental factors and emotional well-being on fatigue perception and underscores the role of oxidative stress in the development of fatigue [24].

Deep breathing exercises were implemented in both intervention and control groups, with a focus on abdominal and thoracic breathing [25]. Group B, which received these interventions, demonstrated significant improvements in fatigue levels and various aspects of quality of life [22]. Flexibility exercises, which enhance blood flow to tissues and muscles, were found to play a crucial role in improving patients' well-being [26]. Stretching exercises promote not only injury prevention but also rehabilitation. The study emphasizes the importance of stretching to enhance flexibility and overall joint health [26].

The findings point to a noteworthy improvement in fatigue levels and HRQoL among the interventional group following the 6-week innovative exercise regimen, as compared to the control group [27]. These results are in harmony with prior research, indicating the effectiveness of diverse exercise protocols in addressing PDFS. GET emerged as a crucial element within the intervention, demonstrating its efficacy in mitigating fatigue and enhancing physical functionality [27].

This study aligns with the findings of previous research on treatments for chronic fatigue syndrome (CFS) [28]. It supports the effectiveness of GET, which was performed in line with deconditioning and exercise intolerance theories [29]. The intervention aimed to gradually reintroduce patients to appropriate physical activity to reverse deconditioning, leading to reduced fatigue and disability [27]. However, this study demonstrated significant improvements within groups, and the outcome measures showed notable enhancements in PDFS.

In addition, the research conducted a comparative analysis with previous investigations involving adaptive pacing therapy, cognitive behavior therapy, and specialized medical treatment for CFS [28,29]. The amalgamation of adaptive pacing therapy, specialized medical care, cognitive behavior therapy, and GET demonstrated greater efficacy in alleviating fatigue and enhancing physical functionality when contrasted with the utilization of adaptive pacing therapy or specialized medical care in isolation. Nevertheless, it is crucial to acknowledge that the study identified limitations pertaining to sample size and the potential presence of biases.

The findings were consistent with other studies indicating that GET is an effective treatment for CFS [30]. It emphasized the importance of "starting low and going slow" in activities and exercise for individuals with PDFS [30]. The study also recommended that further research should explore exercise technique modifications to enhance the lives of those with PDFS/CFS [25].

Although this study provided valuable insights, it was constrained by certain limitations, including a limited sample size, the absence of extended-term follow-up, and its confinement to a particular geographic region. The study provides essential baseline information and supports the effectiveness of innovative exercise protocols in improving PDFS and overall quality of life. Further randomized controlled trials with larger sample sizes are recommended to enhance our understanding of PDFS and its treatment.

The study highlights the positive impact of innovative exercise protocols, GET, and deep breathing exercises on reducing fatigue and improving quality of life. The findings have clinical implications for physiotherapists and the broader population suffering from CFS or PDFS. Future research should continue to explore exercise techniques and methodologies to enhance the lives of individuals with PDFS/CFS and provide a broader perspective on therapeutic outcomes in clinical practice.

CONCLUSION

This study has contributed to our understanding of PDFS and potential treatment options. Employing a randomized controlled trial, we assessed the influence of inventive exercise regimens on individuals with PDFS, uncovering that physical activity effectively diminishes fatigue and improves the quality of life in terms of health-related aspects (HRQoL). Both experimental and control groups experienced reduced fatigue levels and improved HRQoL, with the innovative exercise protocol yielding even more substantial benefits. However, surface fitting and grasshopper components showed no significant improvement, suggesting a need for tailored approaches. This study underscores the potential of exercise interventions in managing PDFS and provides a foundation for future research in this area.

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CONFLICTS OF INTEREST

Nil.

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