ORIGINAL ARTICLE

The Impact of Obesity on Generalized Fatigue in Knee Osteoarthritis: An ANCOVA Study Controlling for Pain Intensity in Malaysia

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ABSTRACT

Introduction: Knee osteoarthritis (KOA) is a painful degenerative joint disorder that is becoming more prevalent because of the ageing population, obesity, and sedentary lifestyles worldwide. Both generalized fatigue and obesity are highly prevalent in the KOA population, however, limited research exists on the effect of obesity on generalized fatigue in this population. Therefore, the current study aimed to investigate the relationship between obesity and generalized fatigue among individuals with KOA. **Methods:** A cross-sectional study was conducted involving 80 KOA participants recruited from two physiotherapy clinics, and categorized into obese (BMI ≥ 23 kg/m^2) and non-obese (BMI ≤ 22.9 kg/m^2) groups. Generalized fatigue was evaluated using both subjective and objective measures. The Fatigue Severity Scale (FSS) was used to assess self-perceived fatigue, and the Six Minute Walk Test (6MWT) was used to measure objective fatigability. A one-way ANCOVA was conducted to compare these variables between obese and non-obese participants, with pain intensity as a covariate. **Results:** The prevalence of self-perceived fatigue was 65%. The mean FSS score was 39.37 ± 15.80, and the mean fatigability score was 21.27 ± 11.63%. The obese group reported significantly higher mean scores for self-perceived fatigue (42.33), and fatigability (23.77) compared with the non-obese group (35.58, 16.38 respectively). **Conclusion:** Obesity was associated with increased levels of both self-perceived fatigue and fatigability, independent of pain intensity. These findings highlight the importance of weight management in addressing generalized fatigue among KOA patients. Future research should explore the potential weight management interventions to reduce fatigue in individuals with KOA.
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Keywords: Knee osteoarthritis (KOA), generalized fatigue, obesity, body mass index (BMI), ANCOVA

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INTRODUCTION

Knee osteoarthritis (KOA) is a common musculoskeletal disorder and a leading cause of pain and disability, particularly in older adults (1). An estimated 10% of adults over the age of 60 years suffer from KOA due to increased life expectancy, lack of physical activity, and obesity (2). Obesity, often defined by an increased body mass index (BMI), is a chronic, multifactorial condition characterized by an excessive accumulation of body fat that significantly increases the risk of KOA through increased mechanical stress on the joints and systemic inflammatory processes (3). According to recent global estimates, approximately 13% of the world's adult population suffers from obesity (4). Given that obesity rates have surpassed the prevalence of KOA, it is crucial to prioritize effective strategies to prevent and manage obesity, as this is a key factor in reducing the burden of KOA (5).

The experience of chronic pain and disability in patients with KOA is often accompanied by generalized fatigue, which is defined as the feeling of constant tiredness or exhaustion (6). In KOA, generalized fatigue can arise from various factors, such as chronic pain, disrupted sleep patterns, and other underlying health conditions like systemic inflammation and psychological distress (7). Studies have reported a high prevalence of generalized fatigue among the KOA population, with estimates ranging from 49% to as high as 81.5% (7,8).

Despite its high prevalence, generalized fatigue in KOA has received less attention in research and clinical practice (9). This oversight may be due to the fact that previous studies assessing fatigue involved participants with other rheumatic conditions; mixed populations with contrasting OA conditions like OA of the hip, knee, and/or hand; or frequently used other clinical populations like fibromyalgia and RA, which constituted a small proportion of individuals with KOA (6). Furthermore, there is no standard definition of fatigue specific to the KOA population, indicating a need for a more comprehensive understanding and assessment of this symptom in KOA rehabilitation (10).

Another major limitation in current research on generalized fatigue within the KOA population is the overemphasis on self-perceived fatigue measured through questionnaires (6). Self-perceived fatigue is subjective and influenced by various factors, such as mood and sleep quality, potentially leading to an underestimation of the true extent of generalized fatigue (11). To address this limitation, the concept of fatigability has emerged as a more objective assessment of generalized fatigue (12). Fatigability refers to the level of tiredness experienced during physical activity and provides a more standardized measure of fatigue (13). However, few studies have specifically investigated fatigability within the KOA population, highlighting a significant research gap (14).

Moreover, the inflammation associated with obesity can also cause generalized fatigue, yet there is a gap in understanding the influence of increased BMI on generalized fatigue among the KOA population (6). Studies on other chronic conditions, such as rheumatoid arthritis and fibromyalgia syndrome, have found associations between increased BMI and higher fatigue severity (15,16). These findings highlight the need to investigate the relationship between increased BMI and generalized fatigue in patients with KOA, particularly considering the high prevalence of obesity in this population (17).

Given these gaps in the current literature, the current study aimed to analyze the impact of obesity on generalized fatigue by comparing self-perceived fatigue and fatigability scores between obese and non-obese individuals with KOA while controlling for pain intensity as a covariate. Pain is a primary symptom of KOA and is known to significantly influence both fatigue levels and physical function (6). Moreover, pain intensity can vary greatly among KOA patients and may not always correlate directly with BMI or radiographic severity of the disease (18). Therefore, to isolate the specific impact of obesity on generalized fatigue, pain was used as a covariate in the current analysis. This approach enabled a more nuanced understanding of how obesity contributes to generalized fatigue in KOA, beyond the influence of pain.

By addressing these objectives, the current study aimed to provide a more comprehensive understanding of the complex interplay between obesity and generalized fatigue in KOA, potentially informing more effective treatment strategies and improving patient outcomes. The findings of the current study are valuable for researchers, clinicians, physiotherapists, and all members of the healthcare team involved in treating individuals with KOA.

MATERIALS AND METHODS

Study Design and Participants

The current study employed a cross-sectional approach and adhered to the recommendations outlined in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement (19). The study settings were the Physiotherapy Clinic, Faculty of Health Sciences, UiTM, and Klink Kesihatan Seksyen 19 Shah Alam, Malaysia. The purposive sampling was chosen to ensure the selection of participants who met the inclusion criteria. Researchers use this sampling technique when gaining deeper insights, exploring rare traits, or investigating special study populations and groups (20). Moreover, this sampling technique was both cost-effective and time-effective and provided maximum variation for the inclusion of study participants. Individuals diagnosed with KOA between January and April 2020 who visited either of the research settings and met the inclusion were selected for the current study.

The ethics approval for the current study was obtained from the research ethics committee of the University Teknologi MARA (UiTM), Malaysia (600-IRMI-5/1/6). Each individual allocated for research was ensured to undergo the consent-taking process. Before collecting data, each participant understood the process and purpose of the research along with details regarding the privacy and confidentiality of the participants and risk as well as benefits to participation. In addition, participants were allowed to withdraw at any time and could be discontinued from participating due to any medical reasons without penalty.

Inclusion and Exclusion Criteria

The current study included both male and female participants aged 50 years and above, who were diagnosed with KOA. The diagnosis of KOA could be based on either reported symptoms or confirmed through radiographic imaging, such as X-rays or MRI scans. To ensure clear communication and informed participation, the current study included only individuals who were able to understand and follow instructions regarding testing procedures delivered in either Malay or English. Those individuals who presented any major injury to the lower extremities, especially at the hip and knee joints, or those with a post-surgical history of knee or hip joint were ruled out as ineligible for this study (21). In addition, participants who had any congenital or developmental deformities of lower extremity joints, especially the deformities of knee joints like genu **velum**, genu varum, genu recurvatum, congenital dislocation of the knee joint, and congenital ankylosing of the knee were excluded from this study (22).

Body Mass Index Classification

The reference values for BMI were adopted from the Asia-Pacific Body Mass Index System because these values are specific to Asian people and were previously employed in various relevant studies in Malaysia (23). A BMI greater than or equal to 23 kg/m^2 was selected for the obese group and a BMI less than 23 kg/m^2 was referred to the non-obese group. While BMI is a widely used indicator of obesity, it has limitations because it does not differentiate between fat and muscle mass (23). The reference values used for BMI classification according to the Asia-Pacific body mass index system are listed in **Table I**.

Table I: Asia-Pacific Body Mass Index Classification System

Classification	Body Mass Index (kg/m^2)
Underweight	<18.5
Normal	18.5–22.9
Overweight	23–24.9
Obese	≥25

Clinical Diagnosis of Knee Osteoarthritis

The American Rheumatism Association (ACR) criteria have been used in the current study for KOA diagnosis. The ACR criteria have three different sections (24). The pain section assesses the presence and location of knee pain (25). The physical function section assesses the limitations of daily activities related to knee function (24). The third section focuses on radiographic findings of joint space narrowing and osteophytes (26).

The ACR criteria have been validated as a specific and reliable tool for KOA diagnosis (27). The radiological section of the ACR criteria could not be employed in the current study because individuals in both study settings did not have radiological findings reports such as x-rays or other scans and had orthopedic referrals. Instead, the diagnosis of KOA was based on a thorough evaluation according to the first two sections of the ACR criteria which comprised history and physical examination of the knee joint. This criterion is mainly based on the history of the KOA patients and their clinical examination. According to this criterion, if a person has knee pain and any of the following three conditions, then the diagnosis of KOA is confirmed (27).

- Over 50 years of age
- Less than 30 minutes of morning stiffness
- Crepitus in active motion
- Bony tenderness
- Bony enlargement
- No palpable warmth of synovium

Generalized Fatigue

Generalized fatigue was evaluated using both subjective and objective measures. For subjective assessment, participants completed a validated questionnaire named as the “Fatigue Severity Scale” (FSS) to assess their self-perceived fatigue. This questionnaire measures participant’s fatigue experience over the past week. The FSS is a frequently used inventory for the evaluation of generalized fatigue among the elderly population as well as the KOA population (7). The FSS demonstrated satisfactory validity and high reliability with an intraclass correlation coefficient (ICC) of 0.949 (23). While the validity and reliability of the FSS have been established in prior research, a formal pilot study was not conducted in the current research, recognizing its limitations and the need for further validation specific to the target population.

The FSS comprises nine statements that participants use to rate their self-perceived fatigue severity (28). Each statement was rated on a 7-point Likert scale. This 7-point Likert scale ranged from 1 to 7, where 1 indicated strong disagreement and 7 indicated strong agreement for each statement of the scale (29). Participants rated their level of agreement with each statement, reflecting their perceived severity of fatigue.

In the FSS, the minimum possible score is 9 and the maximum is 63. Scores closer to 63 reflect a higher level of self-perceived fatigue, whereas lower scores (closer to 9) indicate minimal perceived fatigue (30). According to the established guidelines for scoring the results for this scale, a score of 36 and above (out of a maximum of 63) indicates the presence of significant fatigue (21). However, in the current study, the sum of the total score was also calculated to determine the mean values and standard deviations.

For the objective assessment of generalized fatigue, fatigability was assessed by observing a reduction in walking speed, followed by the six-minute walk test (6MWT) and for visual representation **Figure 1** can be referred. Although traditionally used to measure exercise capacity and endurance, the 6MWT has also been validated for assessing fatigability in older adults (31). In the 6MWT, a decline in walking speed serves as a marker of fatigability (31,32). For example, a previous study observed a 4.6% decrease in walking speed (meters/second) between the first and last minutes of the 6MWT, indicating fatigability (33).

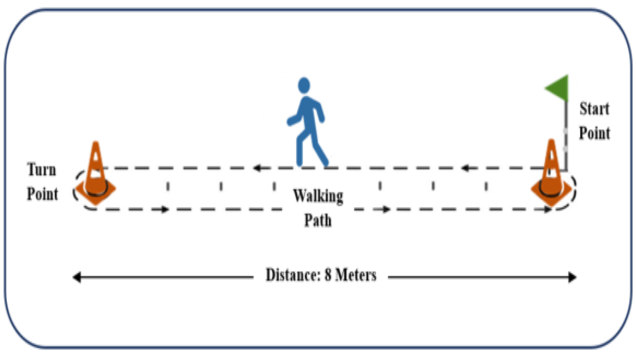

Fig. 1: Six-Minute Walk Test 6 (6MWT) Path

Hence, the present study also employed this test as a secondary measure to evaluate generalized fatigue over a specific period. The 6MWT was chosen as the secondary measure for several reasons. Firstly, previous research has demonstrated its effectiveness in assessing both fatigability and exercise capacity within the KOA population (34). Secondly, studies have shown excellent test-retest reliability for the 6MWT in KOA patients, with an ICC of 0.99 (35). Moreover, the 6MWT complements the subjective information obtained from the FSS, providing a more comprehensive picture of generalized fatigue in the current study.

During the 6MWT, the distance covered by the participants was recorded in meters at each minute interval. The walking speed was then calculated by dividing the distance covered in each minute by the corresponding time. A key indicator of fatigability in the current study was the difference in walking speed between the first and last minute of the 6MWT. A greater decrease in speed indicated a higher level of fatigability (32). Before performing this test, it was ensured that each participant could perform the test without any potential risk. A review of each participant's medical history and physical examination ensured their fitness for the test. A designated walking area was marked on the floor using two cones placed 8 meters apart. Participants were required to turn around the cones.

Each participant was given clear instructions on performing the 6MWT. This involved providing verbal instructions that explained the walking area layout, proper walking technique, and rest allowances. To enhance comprehension, researchers offered individual demonstrations for participants who required further clarification or who might have had difficulty understanding the verbal instructions. These demonstrations visually illustrated the proper walking path around the cones, the pivoting techniques for efficient turns, and the resting procedures.

Participants were asked to walk back and forth around the cones for six minutes as illustrated in Fig.1. They were allowed to stop, slow down, and lean against the wall or sit on a chair to rest as many times as they wanted in case they got out of breath or became exhausted. They were asked to resume walking as soon as they could walk again. However, during rest, the timer was still counting on the stopwatch. Participants were asked to pivot briskly around the cones and continue walking back to the other cone without hesitation. None of the participants used any walking aids. While the participants were walking, the researcher was walking a step behind them, following their pace to note down the distance. When the test was completed, the participants were asked to stop and stand still at their final location to note the total distance covered.

Data Collection and Interpretation

Recruitment involved contacting newly referred KOA patients at both clinics and scheduling appointments for those who expressed interest in taking part in the current research. All participants provided informed consent before their involvement in the study. Upon initial contact, 110 potential participants were screened for eligibility, based on pre-defined inclusion and exclusion criteria. This process identified eligible participants for further involvement in the research. Out of the 110 individuals screened, 80 were selected for the current study. The remaining 30 individuals were excluded for not meeting the inclusion criteria or for declining participation. The final enrolled sample consisted of 70 females and 10 males, resulting in 80 participants, which was the desired sample size for the current study (N=80).

Following confirmation of eligibility, the researchers contacted the participants to schedule a convenient time for their participation in the study. Data collection occurred during a single in-person visit to the research facility. At the beginning of the study, participants completed a structured assessment form to gather information on their socio-demographic background and medical history. Common demographic features such as age, gender, ethnicity, marital status, employment status, education, and relative medical history such as knee pain were observed.

For anthropometric data, body weight and height were measured. Body weight was determined using a digital weight scale in kilograms (kg), whereas height was measured in meters (m) using a stadiometer. Participants were ensured to be wearing light clothing and no high-heeled shoes. The BMI was calculated by dividing the weight in kilograms by the height in square meters (kg/m^2). Generalized fatigue was assessed using two methods (FSS and 6MWT), taking approximately 10-15 minutes.

Following data collection, the main researcher comprehensively reviewed all questionnaires and assessment forms for completeness and accuracy. Any missing data points were documented, and attempts were made to collect missing information from participants, if feasible. All participant data were anonymized by assigning a unique serial number and then was entered into SPSS (Statistical Package for Social Sciences) version 26 for analysis.

Descriptive statistics were used to summarize participant's demographics. This included measures such as means, standard deviations, frequencies, and percentages. Prior to statistical analysis for each objective, the normality of the data, particularly for continuous variables, was assessed to ensure adherence to the assumptions of the planned tests. A Shapiro-Wilk test was conducted to statistically evaluate the normality of the data distribution. Data met the normality assumptions (p-value>0.05), allowing for parametric tests. The first objective was to characterize generalized fatigue (self-perceived fatigue and fatigability). Descriptive statistics, including means values, standard deviations, frequencies, and percentages were calculated for these variables in a sample of 80 participants.

For the second objective of the current study which was to investigate the impact of obesity on generalized fatigue, participants were categorized into the obese and non-obese group. ANCOVA (Analysis of Covariance) was performed to compare the means of these variables between the two groups while controlling for the effects of pain intensity. Obesity status (whether obese or non-obese) was the independent variable, whereas generalized fatigue was the dependent variable. The ANCOVA assumptions regarding the homogeneity of regression slopes, homogeneity of variances, and normality of residuals were rigorously tested to ensure the analysis's integrity and the reliability of the results.

RESULTS

Socio-demographic Characteristics

Out of 80 participants, 12 were from the Physiotherapy Clinic, UiTM, Puncak Alam, while the other 68 were from Klinik Kesihatan Seksyen 19, Shah Alam. There were 53 obese (BMI ≥ 23 kg/m^2) and 27 non-obese (BMI ≤ 22.9 kg/m^2) participants. The socio-demographic characteristics of the total study population and group comparison are presented in Table II. In terms of age, the results showed that out of 80 participants, 39 (48.8%) belonged to the 60-69 years age group, 14 (26.4%) belonged to 50-59 years age group. While 12 (22.6%) participants were ≥ 70 years. The mean age of 80 participants was 62.6 ± 7.10. The mean age reported for the non-obese group (59 ± 6.02) was lower than the obese group (64.434 ± 6.95). Results also showed that females made up the vast majority of the participants as 70 (87.5%) participants were females. The group comparison showed that the non-obese group comprised 12 (66.7%) females and the obese group had 58 (98.1%) females.

The ethnic distribution showed that most of the participants were Malays. Out of 80 participants, 59 (73.8%) were Malays. The non-obese group comprised 44 (83%) Malays, whereas the obese group comprised 15 (55.6%) Malays. The marital status showed that 62 (77.5%) participants were married, of which 20 (74.1%) belonged to the non-obese group and 42 (79.2%) to the obese group.

The majority of the study population had a secondary education level (n=41, 51.2%), whereas five participants (6.3%) had no formal schooling. The non-obese group

Table II: Socio-demographic Characteristics of the Total Study Population, and Comparisons between Obese and Non-obese Participants with Knee Osteoarthritis

Variable	Total Study Population (N=80)		Non-obese group (n=27)		Obese group(n=53)		*P*-value
	Mean ± SD (Range)	n (%)	Mean ± SD	n (%)	Mean ± SD	n (%)	
Age (years)	62.6 ± 7.1		59.00 ± 6.02		64.43 ± 6.94		0.659[a]
50-59	(50-81)	28 (35.0%)		14(51.9%)		14(26.4%)	
60-69		39 (48.8%)		12(44.4%)		27(50.9%)	0.025[b]
≥ 70		13 (16.3)		1(3.7%)		12(22.6%)	
Gender							
Male		10 (12.5%)		7(26%)		3(5.7%)	< 0.001[b]
Female		70 (87.5%)		20(74.1%)		51(96.2%)	
Race							
Malay		59 (73.8%)		15(55.6%)		44(83.0%)	0.008[b]
Non-Malay		21 (26.3%)		12(44.4%)		9(17.0%)	
Marital Status							
Married		62 (77.5%)		20(74.1%)		42(79.2%)	0.197[b]
Divorced/Separated		11 (13.8%)		5(18.5%)		6(11.3%)	
Widowed		7 (8.8%)		2(7.4%)		5(9.4%)	
Education Level							
No formal schooling		5 (6.3%)		2(7.4%)		3(5.7%)	
Primary		13 (16.3%)		4(14.8%)		9(17.0%)	0.942[b]
Secondary		41 (51.2%)		13(48.1%)		28(52.8%)	
Tertiary		21 (26.3)		8(29.6%)		13(24.5%)	
Employment Status							0.003[b]
Pensioner		10 (12.5%)		5(18.5%)		5(9.4%)	
Employed		28 (35.0%)		15(55.6%)		13(24.5%)	
Unemployed		42 (52.5%)		7(25.9%)		35(66.0%)	
Pain Intensity	6.08 ± 2.02		3.70 ± 1.20		7.04 ± 1.52		0.031[a]
Mild	(2-10)	13(16.3%)		12(44.4%)		1(1.88%)	< 0.001[b]
Moderate		38(47.5%)		13(48.1%)		25(47.1%)	
Severe		29(36.25%)		1(3.7%)		28(52.8%)	
BMI (kg/m^2)	29.15 ± 6.41 (19.95-41.30)		21.92 ± 0.88		31.24 ± 5.95		< 0.001[a]

SD = Standard deviation; n (%) = Frequency; a = Independent t test (significant at p<0.05); b = Chi square test (significant at p<0.05) had 13 (48.1%) participants with secondary education, whereas the obese group had 28 (52.8%) participants with secondary education. The results further revealed that most of the participants were unemployed (n=42, 52.5%). In the non-obese group, the majority of respondents were employed (n=15, 55.6%), whereas in the obese group, the majority (n=35, 66%) were unemployed.

The mean pain intensity of the total study population was 6.08 ± 2.02, ranging from mild, moderate to severe pain. Out of 80 participants, 38 (47.5%) reported moderate pain, 29 (36.2%) reported severe pain and 13 (16.3%) reported mild pain. The results for the group comparisons for pain intensity revealed substantial disparities, with the obese group experiencing a significantly (p-value = 0.03) higher mean score (7.03 ± 1.51) compared to the non-obese group (3.70 ± 1.20). Moreover, in the obese group, 28 participants (52.8%) reported severe pain intensity, whereas only one participant (3.7%) in the non-obese group experienced severe pain. The participants had a mean BMI of 29.15 ± 6.41 kg/m. The mean BMI of the obese group (31.24 ± 5.95 kg/m) was significantly (p-value < 0.001) higher than that of the non-obese group (21.92 ± 0.88 kg/m).

Assessment of Generalized Fatigue (N=80)

The mean self-perceived fatigue score was 39.37 ± 15.80, with 52 participants reporting a score ≥ 36 on the fatigue severity scale (FSS), indicating a 65% prevalence of generalized fatigue in the current study population. Fatigability, calculated as the percentage of reduction in walking speed between the first and last minute of the six-minute walk test, showed a mean score of 21.27 ± 11.63.

Comparison of Generalized Fatigue between the Obese and Non-Obese Groups of Individuals with Knee Osteoarthritis

Comparison of Self-Perceived Fatigue

To ensure the validity of subsequent statistical tests, data normality was assessed using the Kolmogorov-Smirnov test (p<0.05). The self-perceived fatigue score showed a p-value of 0.18, hence, parametric testing was deemed appropriate. In order to determine if the relationship between pain intensity and self-perceived fatigue score varied substantially as a function of obesity status, a test of slope homogeneity was performed. The results of this test were not significant [F (1,76) = 0.13, p = 0.72], assuming that the slopes were uniform. A one-way ANCOVA was performed as a result.

Levene's test result was non-significant with a p-value of 0.53, demonstrating homogeneity of variation in self-perceived fatigue score across the two groups. The adjusted mean for self-perceived fatigue score was 42.33 in the obese group and 33.55 in the non-obese group, despite pain intensity being adjusted to 5.9, as shown in **Table III**.

Table III: Between Group Comparison of Self-Perceived Fatigue

Groups	n	Unadjusted Mean ± SD	Adjusted Mean
Non-obese	27	24.24 ± 9.65	33.55[a]
Obese	53	47.07 ± 12.43	42.33[a]

a: Covariate appearing in model is evaluated at the following value: Pain intesity = 5.9

As shown in **Table IV**, there was a significant difference in self-perceived fatigue score between the obese and non-obese groups [F (1,77) = 4.638, p= 0.034] with moderate effect size as demonstrated by the partial eta squared value (ηp^2 = 0.57). The partial eta squared value (ηp^2) is the measure of effect size that depicts the impact of the independent variable on the dependent variable and classified as weak when ηp^2 = 0.1-0.3, moderate when ηp^2 = 0.4-0.6, and high when ηp^2 = 0.7-1 (36). Results shows that 57% variance in self-perceived fatigue score is affected by obesity status while controlling for pain intensity.

Table IV: ANCOVA Results for Self-Perceived Fatigue Difference Between Obese and Non-Obese Group

Source	Mean Square	df	F	p-value	$\eta^p 2$
Pain intensity	2046.96	1	18.75	< 0.001	0.196
Obesity status	506.26	1	4.64	0.034	0.57
Error	119.15	77			

Note: R^2 = 0.58 (Adjusted R^2 = 0.56)

Comparison of Fatigability

Given that the fatigability score demonstrated a p-value of 0.314 for normality assessment, parametric testing was deemed appropriate. The slope homogeneity test was conducted to determine if the relationship between pain intensity and fatigability score differed significantly with obesity status, which showed non-significant results [F (1 76) = 0.29, p = 0.60], assuming that the slopes were uniform so the data analysis proceeded for one-way ANCOVA.

Levene's test result was non-significant (p=0.09), demonstrating homogeneity of variation in fatigability across the two groups. The adjusted mean fatigability score was 23.77 in the obese group and 16.38 in the non-obese group, despite pain intensity being adjusted to 5.9, as shown in Table V.

Table V: Between Group Comparison of Fatigability

Groups	n	Unadjusted Mean ± SD	Adjusted Mean
Non-obese	27	8.76 ± 4.79	16.38[a]
Obese	53	27.65 ± 8.43	23.77[a]

As shown in Table VI, there was a significant difference in fatigability score between obese and non-obese groups [F (1,77) = 9.45, p = 0.003] with small effect size as demonstrated by the partial eta squared value ($\eta p2$ = 0.11). Additionally, when pain severity was taken into account, it demonstrated that obesity status had an impact of 11% variance in fatigability score.

Table VI: ANCOVA Results for Fatigability Difference Between Obese and Non-Obese Group

Source	Mean Square	*df*	*F*	*p-value*	η_p^2
Pain intensity	1375.20	1	36.30	< 0.001	0.32
Obesity status	357.93	1	9.45	0.003	0.11
Error	37.88	77			

Note: R^2 = 0.73 (Adjusted R^2 = 0.72)

DISCUSSION

The current study investigated the prevalence of self-perceived fatigue among individuals with KOA in Malaysia, revealing a high prevalence, with 65% of participants reporting generalized fatigue. The reported prevalence of fatigue in the current study differs from the findings of previous studies. For instance, studies have documented prevalence rates ranging from 49% in the USA (8) to 81.5% in Turkey (7). This variation might be due to many factors such as differences in sample characteristics and measurement tools. For instance, both aforementioned studies (7,8) utilized a different fatigue assessment tool (VAS-F) compared to the one used in the current study (FSS).

Research suggests that measurement tools used in different studies can influence the reported prevalence of the condition (37,38). These tools are subjective in nature and can be influenced by the mood and perception of the individuals, potentially leading to an underestimation of the true extent of fatigue (11). Furthermore, the current study participants had a comparatively lower mean score for pain intensity (6.08 ± 2.02) than the participants (7.68 ± 1.77) in the study by Fertelli & Tuncay (7). A previous study reported a positive correlation between KOA pain and fatigue, suggesting that fatigue prevalence is associated with higher pain intensity (39). The lower prevalence of fatigue (65%) in the current study compared with the 81.5% reported by Fertelli & Tuncay (7) might be explained by the difference in pain intensity scores between the studies. Furthermore, potential sociocultural factors and healthcare practices in different regions might play a role, although further research is needed to explore this aspect in more detail (7).

The results of the current study also showed that the overall study participants had a mean score of 39.37 ± 15.80 for self-perceived fatigue, which was higher than the findings (23.88 ± 11.51) of a previous study conducted in Malaysia (31). A potential explanation for these contrasting results may lies in the characteristics of the study participants. The current study's participants had a higher mean age (62.6 ± 7.1 years) compared with Mood et al (20), whose participants had a mean age of 54.76 ± 5.54 years. Research suggests a possible connection between increased age and higher fatigue prevalence among older adults (40). Age-related factors, such as chronic pain, depression, decline in cellular repair, poor sleep quality, and chronic low-grade inflammation, might worsen fatigue by impacting energy levels, lack of motivation, and reduced functional capacity (41). However, further studies are necessary to confirm these associations among individuals with KOA. Additionally, the participants of the current study reported experiencing greater pain intensity (6.08 ± 2.02) compared with the lower pain intensity (1.97 ± 1.59) reported by Mood et al (20). Increased pain causes impairment in muscle function, which can lead to muscle fatigue, thereby decreasing functional performance and increasing generalized fatigue levels (39). These differences in pain intensity scores may have led to the increased mean fatigue score in the current study population.

The results of the current study further revealed the evidence of fatigability which reveals a novel aspect of the Malaysian KOA population by demonstrating a substantial decline in walking speed as a potential indicator of fatigability. This finding is consistent with a recent study by Waqar et al (14) that documented greater fatigability in individuals with KOA. Chronic pain and inflammation in KOA, as suggested by Waqar et al (14) might contribute to fatigability via deconditioning and sleep disruption.

Fatigability refers to how tired someone gets during specific activities, like the 6MWT used in the current study (13). The importance of using this distinct objective measure for generalized fatigue is crucial (42). A previous study argued that relying solely on self-reported fatigue may not capture the full extent of generalized fatigue (43). As per the argument of the aforementioned study, two individuals might report the same level of self-perceived fatigue while having different physical activity levels, but the one with a more restricted lifestyle due to fatigue likely experiences higher fatigability (43).

Several published studies have addressed fatigability among older adults, but few have specifically investigated fatigability within the KOA population, highlighting a significant research gap (14). In Malaysia, Mood et al. (21) focused on self-reported fatigue among the KOA population. This subjective approach for measuring generalized fatigue could be influenced by various factors, such as the individual's perception of fatigue, demographic characteristics of the study population, differences in measurement tool, and selection of cut-off points defining fatigued from non-fatigued (44).

The results also revealed a statistically significant difference in the self-perceived fatigue score between the obese and non-obese groups. The obese group reported a higher mean score compared than the non-obese group. This finding is particularly noteworthy because it contributes to the understanding of generalized fatigue in KOA by demonstrating a significant association between obesity and self-perceived fatigue. Obesity can contribute to fatigue through several mechanisms. Chronic low-grade inflammation, a hallmark of obesity, disrupts sleep and energy production, ultimately contributing to fatigue (45). Moreover, the additional strain on the knees due to carrying extra body weight makes even simple activities more tiring (16). Finally, psychological factors like depression and anxiety associated with obesity further contribute to fatigue and decreased motivation for physical activity (46).

Notably, after controlling for pain intensity as a covariate, the adjusted mean score for self-perceived fatigue in the obese group (42.33) slightly decreased, whereas it increased in the non-obese group (33.55). This finding suggests that pain intensity might not be the sole factor influencing fatigue and there might be other factors that contributed to fatigue score variations between the obese and non-obese groups. Further investigation into these potential factors is warranted in future studies.

In terms of fatigability, the obese group reported significantly higher unadjusted mean scores than the non-obese group. The significantly higher fatigability scores in the obese group suggest a strong association between obesity and fatigability. This finding adds to the limited research on fatigability in the KOA population, particularly because no prior studies have explored this association in Malaysia (6,21). Notably, a study comprising knee or hip OA patients found a strong positive association between BMI and fatigability, supporting the potential link observed in the present study (47). An increase in BMI can lead to greater fatigability through inflammation, disrupting the body's ability to produce energy and increased pain (48).

Interestingly, after controlling for pain intensity, the pattern of fatigability scores between the obese and non-obese groups shifted. The adjusted mean fatigability score in the obese group decreased slightly, whereas it nearly doubled in the non-obese group. This finding suggests that pain intensity does not fully explain the observed differences in fatigability scores across both groups. There are likely other factors contributing to the more pronounced increase in fatigability scores among the non-obese participants after controlling for pain intensity which require further investigations.

Given the cross-sectional design of the current study, the causes of this unexpected shift in fatigability scores could not be definitively determined. However, factors beyond pain intensity, such as the observed differences in mean age between the obese and non-obese groups, might play a role. The mean age of the obese group was higher than that of the non-obese group. A previous study suggested the age-related increase in fatigability; however, the underlying mechanism remains unknown (49).

A significant strength of the current study is its comprehensive approach, which employed both subjective and objective measures of generalized fatigue. To the best of authors' knowledge, this methodological approach is not only rare in the international research landscape but also represents the first such investigation conducted in Malaysia. By combining a comprehensive assessment of generalized fatigue with an examination of the impact of obesity, the current study provides a holistic evaluation of fatigue in KOA patients, addressing a critical gap in the existing literature.

Despite successfully fulfilling its objectives and contributing valuable insights for the KOA population, the present study has limitations, such as its cross-sectional design, unequal gender ratio and both groups' sample size. Hence, future longitudinal studies are warranted with a large sample size comprising identical groups of obese and non-obese participants with KOA. This approach can help establish a comparison group of participants with similar demographics and gender ratios, allowing for more accurate analysis and conclusions regarding the relationship between obesity and generalized fatigue.

CONCLUSION

Results showed a high prevalence (65%) of generalized fatigue among the Malaysian KOA population. Obese KOA participants reported significantly higher levels of both self-perceived fatigue and fatigability than non-obese participants. This difference remained even after adjusting for pain intensity, suggesting that obesity has a substantial independent effect on generalized fatigue. These findings underscore the importance of addressing weight management as a potential target for reducing generalized fatigue in the KOA population.

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