Fatigability And Quality Of Life In Type 2 Diabetes Mellitus Patients With And Without Diabetic Peripheral Neuropathy

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Research Article

Keywords: Quality of Life, Fatigability, Diabetes Mellitus, Diabetic Peripheral Neuropathy.

Posted Date: March 11th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1431189/v1

Abstract

Objectives: Physical fatigue and quality of life (QoL) characteristics in type 2 diabetes mellitus (T2DM) patients may or may not be influenced by long-term complications such as diabetic peripheral neuropathy (DPN). The purpose of the study was to investigate the association between muscle fatigability and QoL concerns in patients with T2DM with or without DPN.

Methods: This study included sixty male and female subjects with an average age of 56±6.6 years from a diabetic screening clinic. Patients with type 2 diabetes mellitus with peripheral neuropathy (T2DMPN), patients with type 2 diabetes mellitus without peripheral neuropathy (T2DM), and healthy control subjects were randomly assigned to one of three groups (n=20). To assess fatigue, quality of life (QoL), and disability in all groups, the Fatigue Severity Scale (FSS), Short Form survey (SF-36), and Modified Neuropathy Disability Score (MNDS) were used.

Results: FSS and QoL, particularly Physical Component Summary (PCS), were statistically significantly affected in T2DMPN patients as compared to T2DM patients and healthy controls ($p<0.05$). However, the Mental Component Summary (MCS) of QoL was found to be insignificant in all study groups, including healthy controls, T2DM, and T2DMPN ($p>0.05$). Both the healthy control and T2DM groups exhibited nearly identical levels of FSS and QoL, as well as PCS and MCS ($p>0.05$).

Conclusions: T2DM with DPN has a significant impact on fatigability and QoL. This could be because of T2DM's pathological consequences and diabetic management in each demographic cohort. According to the findings, further efforts are needed to prevent or minimize deterioration in physical performance and QoL in T2DMPN patients.

Introduction

Diabetes is a chronic metabolic condition characterized by hyperglycemia caused by the body's inadequate insulin secretion and/or insulin resistance. Diabetes devastates the vascular and nervous systems, resulting in a slew of life-threatening complications. It is widely acknowledged as a global public health emergency [1]. Type-2 Diabetes Mellitus (T2DM) also known as non-insulin-dependent diabetes or adult-onset diabetes is caused by the body's poor utilization of insulin and affects the majority of diabetics [1].

Saudi Arabia has the second highest rate of diabetes mellitus in the Middle East, and one of the highest rates in the world, with an estimated population of 7 million people with diabetes and more than 3 million people with pre-diabetes [2]. If current trends continue, the International Diabetes Federation (IDF) estimates that the number of people living with diabetes in the Middle East would nearly quadruple by 2030 [2]. Excess body weight and physical inactivity are the main causes of this kind of diabetes and is a serious health concern for any country. Unhealthy lifestyles and eating habits have been linked to the development of insulin resistance in the body's cells [3].

Saudi Arabia's rapid economic expansion has endowed the population with an opulent lifestyle, which has led in a decrease in physical activity and the adoption of unhealthy eating habits. In Saudi Arabia, the rising incidence of Type-2 Diabetes Mellitus (T2DM) is closely linked to lifestyle-related risk factors that must be addressed in order to prevent the disease and its complications [3, 4]. Over the years, extensive diabetes research has substantially increased our understanding of the disease's etiology and effects, as well as offered a number of new and improved remedies. Implementing the findings of these studies has resulted in a reduction in chronic complications and mortality in patients with diabetes; yet, there is a paucity of diabetes literature in Saudi Arabia [3].

One of the most prevalent long-term consequences of T2DM is diabetic peripheral neuropathy (DPN). The most common type of DPN is distal symmetrical polyneuropathy, which is characterized by painless paresthesia, loss of ankle reflex, and impairment of vibration, joint position, touch, and pressure sensations. The prevalence of DPN was found to be fairly high over the world, ranging from 36.6 % to 20% in the Middle East [5]. People with T2DM who are aware of the consequences of DPN can assist their caregivers in diagnosing and treating peripheral neuropathy as early as possible. Despite this, there is a scarcity of information in Saudi Arabia about DPN in T2DM patients [6]. Distal symmetrical polyneuropathy's long-term impact on quality of life (QoL) and fatigability should be thoroughly explored for better medical and rehabilitation management.

Traditionally, all healthcare interventions have aimed to improve individual's quality of life and prevent disorders. Diabetes, like other chronic diseases, cannot be totally cured. As a result, ensuring that persons with diabetes have a reasonable quality of life (QoL) is essential [2]. According to existing literatures, the term of QoL comprises the physical, emotional, and social components, and it changes with time and according to the individual's perception [7]. The QoL is a broad concept that encompasses a variety of human needs, such as a human's place in life, objectives, standards, expectations, and concerns in the context of culture and value systems [8]. Furthermore, the great majority of QoL studies have been carried out in regional collaborations, with cross-national collaboration being less common. Despite the large number of topics connected to QoL in various illnesses, investigations on socio-cultural aspects and their impact on QoL appear to be uncommon and it is recommended that cultural issues should be considered when making policy decisions and interactions between developed and developing countries should be encouraged [8]. The QoL indicators are dependable measures of a person's efforts to maintain long-term health, engagement, and productivity [9]. Because of a greater understanding of the impact on patients' QoL, QoL is progressively becoming recognized as an important indication for chronic illnesses, which subsequently leads to better patient management. To assess patient QoL, a variety of tools are currently available. The Short Form 36 (SF36) questionnaire is a widely used tool for assessing QoL. It consists of 35 elements divided into two groups and distributed throughout eight categories, including both physical and psychological dimensions [7].

Identifying variables connected to fatigue and low QoL in patients with DPN should help policymakers prioritize funds and implement QoL-improving measures. Fatigue has been linked to a decrease in physical functioning and impact activities of daily living. The concept of fatigue in people with T2DM

appears to be a little hazy. Diabetic patients are affected by the Diabetes Fatigue Condition (DFS), which is a multifactorial fatigue or easy fatigability syndrome. DFS can be caused by a combination of lifestyle, dietary, medicinal, psychological, glycemic or diabetes-related, endocrine, and iatrogenic factors [10]. Fatigue, regardless of its source, has a negative impact on one's quality of life. Fatigue may be connected to a variety of factors in T2DM patients, including sociodemographic factors, clinical disease, inflammatory factors, psychological stress, behavior and lifestyle choices [11]. When choosing appropriate therapies, these relevant factors should be taken into consideration.

A limited number of investigations have explored the fatigability in DPN patients [11, 12]. However, to our knowledge, there is a scarcity of research that has explored the relationship between DPN severity, general fatigability, and QoL in patients with T2DM particularly in the Saudi Arabian community. The objective of this research were to determine the level of fatigability, severity of DPN and QoL among patients with T2DM with/without DPN, and also to investigate if there was a link between fatigability and QoL.

Material And Methods

Participants

A total of 100 individuals who attended the diabetic screening clinic in a university hospital were screened and a sample of sixty male and female subjects with a mean age of 56±6.6 years and BMI 29±5.3 kg/m^2 selected for the current study. Each participant signed an informed consent form and received a detailed description of the study procedure prior to the start of the evaluation. The Research and Ethics Committee of King Saud University's College of Applied Medical Sciences approved this study, approval no: E-19-3731. Clinical data was collected, including diabetes duration, diabetic complications, smoking, and other comorbidities. None of them had a history of cerebrovascular accidents, ischemic heart disease, lower extremity fractures, congenital and acquired foot deformities, malignancies, or other neuropathies, according to the study's inclusion criteria. All medical information was obtained through patient interviews or from medical records. Patients with type 2 diabetes mellitus with peripheral neuropathy (T2DMPN), patients with type 2 diabetes mellitus without peripheral neuropathy (T2DM), and healthy control subjects were randomly assigned to one of three groups (n=20) based on clinical data and the Modified Neuropathy Disability Score (MNDS). The Fatigue Severity Scale (FSS), Short Form survey (SF-36), and MNDS variables were used to assess and analyses the relationship respectively fatigue, quality of life (QoL), and disability in all groups.

Procedure

Assessment of FSS

Level of fatigue was examined by the Arabic version of the Fatigue Severity Scale (FSS), which is a self-reported questionnaire; composed of 9 statements that measure the extremity of the patient’s fatigue regarding how these symptoms influence motivation, exercise, physical function, and activities of daily

living. The nine statements that describe the severity and impact of fatigue, with responses ranging from 1 to 7 on a scale of 1 (strongly disagree) to 7 (strongly agree). The final score is generally represents the mean value of the nine items; a higher score implies greater severity [13].

Assessment of QoL

The 36-item Short Form survey (SF-36) is commonly considered the gold standard for determining QoL [14]. The SF-36 has 8 multi-item scales assessing physical function (PF) (10 items), physical role-limitation (RP) (4 items), body pain (BP) (2 items), general health (GH) (5 items), energy (VT) (4 items), social function (SF) (2 items), emotional role-limitation (RE) (3 items) and emotional well-being (MH) (5 items). The 8-item scales were used to calculate the QoL scores. The eight item scales were evaluated on a 0 to 100 scale based on the response to each question, according to item response theory. A score of 50 or higher was considered normal, while a score of less than 50 was considered a poor QoL. The lower the score, the more disabled you are (a score of zero is equivalent to maximum disability and a score of 100 is equivalent to no disability). The scores on these eight questions can be broken down into two categories: physical (PCS) and mental (MCS) component summary [14]. The PF, RP, BP, and GH domains were all included in the PCS's pooled mean score. The VT, SF, RE, and MH domains were all included in the MCS's pooled mean score. For patients with T2DM, the SF-36 has been demonstrated to be a reliable and valid test [14, 15].

Assessment of Neuropathy

The severity of neuropathy was determined using the modified Neuropathy Disability Score (MNDS) (score from 0-10). The presence or absence of ankle reflexes, as well as vibration perception (using a 128-Hz tuning fork), pin-prick, and temperature perceptions in the great toe, all contributed to the NDS. Sensory modalities were graded as present (0), decreased or absent (1), and ankle reflexes as normal (0), present with reinforcement (1), or absent (1) for each leg (2). The maximum score is ten, which indicates full sensory loss and the absence of reflexes. The highest possible aberrant score was ten and a score of more than 2 was considered clinical DPN. It is well-known for being a reliable and valid tool for determining the degree of DPN [16].

Data analysis

For data entry and analysis, IBM's Statistical Package for Social Sciences (SPSS version 25.0) was utilized. For qualitative variables, descriptive statistics were derived using frequency and percentage, whereas for quantitative data, mean and standard deviation were used. To compare variables, a one-way ANOVA was employed.

Table 1. Descriptive data for all groups

Study Variables	Control group (n=20)	T2DM group (n=20)	T2DMPN group (n=20)
MNDS	00	00	4±2
FSS	1.3±0.5	1.8±0.4	2.5±0.5
QoL – PF (PCS)	91.5±11	89.8±11	77.7±20
QoL – RP (PCS)	81.3±39	63.8±48	46±52
QoL – BP (PCS)	86.6±17	80.3±25	66.9±31
QoL – GH (PCS)	78.5±15	70.8±16	68.9±17
QoL – VT (MCS)	60.5±22	59.3±25	53.1±28
QoL – SF (MCS)	89.5±16	81.9±31	86.5±22
QoL – RE (MCS)	82±42	81.7±38	73.9±52
QoL – MH (MCS)	80.8±24	80.2±16	81±20

Table 2. MNDS, FSS and QoL multiple comparisons among groups

Study Variables	ANOVA Multiple Comparisons	Control group Vs T2DM	Control group Vs T2DMDPN	T2DM Vs T2DMDPN
MNDS	95% CI	-.67 - -.67	-4.60 - -3.09	-4.60 - -3.09
	Sig.	1.000	.000	.000
FSS	95% CI	-.25 - .35	-.58 - .10	-.63 - .05
	Sig.	.740	.04	.05
QoL – PF (PCS)	95% CI	-6.99 - 10.49	3.97 - 23.65	2.22 - 21.90
	Sig.	.689	.007	.017
QoL – RP (PCS)	95% CI	-11.64 - 46.64	2.27 - 67.93	-50.43 – 0.2
	Sig.	.233	.037	.04
QoL – BP (PCS)	95% CI	-9.04 - 21.54	2.48 - 36.93	-30.68 - 3.77
	Sig.	.416	.026	.050
QoL – GH (PCS)	95% CI	-2.46 - 17.96	-2.85 - 25.16	-0.71 – 0.6
	Sig.	.134	.050	.0.05
QoL – VT (MCS)	95% CI	-14.32 - 16.82	-10.12 - 24.96	-23.71 - 11.37
	Sig.	.873	.399	.483
QoL – SF (MCS)	95% CI	-7.84 - 22.94	-14.42 - 20.25	-12.70 - 21.97
	Sig.	.329	.737	.593
QoL – RE (MCS)	95% CI	-34.06 - 20.76	-9.73 - 52.04	-58.69 - 3.08
	Sig.	.628	.175	.077
QoL – MH (MCS)	95% CI	-19.21 - 6.41	-21.55 - 7.30	-13.70 - 15.15
	Sig.	.320	.326	.920
QoL HC	95% CI	6.43 - 36.07	-4.20 - 29.20	-7.95 -
	Sig.	.610	.139	.298

Results

The MNDS revealed that patients with T2DMPN had substantial peripheral neuropathy, scoring 4±2 out of ten (Table 1, 2).

The FSS results revealed that all groups exhibited varying degrees of fatigue severity. T2DMPN patients, on the other hand, showed a higher level of fatigue than healthy controls and T2DM patients (Table 1).

The patients with T2DMPN had a lower quality of life, particularly in terms of Physical Component Status (PCS), than the healthy controls and the patients with T2DM (Table 1).

The FSS and QoL scores, particularly the Physical Component Status (PCS) (i.e. PF, RP, BP, and GH), were statistically significant in T2DMPN patients compared to T2DM patients and healthy controls ($p<0.05$); however, the Mental Component Status (MCS) of QoL was not statistically different in all groups ($p>0.05$). Furthermore, both the healthy control group and the T2DM patients group exhibited nearly identical levels of FSS and QoL ($p>0.05$). (Table 2)

Discussion

Fatigue and peripheral neuropathy are prominent and distressing concerns in patients with chronic diabetes, and they can make it difficult to accomplish everyday chores. In comparison to patients with T2DM and healthy control groups, the current study found that QoL, specifically Physical Component Summary (PCS) and fatigability, is considerably impacted in patients with T2DMPN. This could be attributed to the obvious clinical symptoms of DPN, such as a high MNDS score in T2DMPN patients. Our findings corroborate a previous study that found widespread DPN damage, notably in sensorimotor polyneuropathy, which is connected to pain, a worse QoL, poor outcome, and higher healthcare costs [17]. Patients with DPN and peripheral artery disease (PAD) causes muscle atrophy, particularly in the lower limb's distal segment, due to their effects on motor nerve impairment and reduced muscle blood flow [18]. Furthermore, DPN and fatigue limit movement, limit everyday activities, and create challenges in family, social, and professional duties. DPN also raises the chance of falling and losing individual's balance while standing or walking [18, 19, 20].

Diabetes mellitus is one of the most difficult diseases to manage since a variety of factors such as physical activity, glucose testing, findings, time from diagnosis, and depression have all been demonstrated to have a significant impact on QoL [4]. Previous research has found that elderly and chronic T2DM patients have a moderate QoL in connection to co-morbidities, as well as limitations in physical functions and the strongest negative relationships with physical score [21]. T2DMPN is a condition that develops as a result of uncontrolled or poorly controlled T2DM for an extended period of time, culminating in the patient becoming a T2DMPN patient. T2DMPN patients with complications had a lower PCS in QoL, which might be attributed to T2DMPN consequences like neuropathy, retinopathy, and cardiovascular disease, which were the three most potent factors linked to poor QoL [22]. Long-term diabetes has been connected to a lower quality of life in previous studies; the PCS was linked to the time since diagnosis, while the MCS was linked to anxiety and depressive symptoms but not to diabetes duration or metabolic control [23]. Because QoL is described as an individual's impression of their place

in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and fears [1,2], it's probable that the MCS component was unaffected. The outcomes of this study suggest that the healthcare system should focus more on physical activity adjustments for patients with T2DMPN in order to lessen the impact of comorbidities on their QoL.

Fatigue is a typical symptom of hyperglycemia in diabetic patients, and it is likely impacted by disease physiology, psychological stress, and lifestyle factors [18,24]. In people with diabetes, fatigue, particularly central weariness, is an uncomfortable condition [24]. Fatigue in skeletal muscle in diabetic individuals is caused by a combination of neurological, musculoskeletal, and metabolic abnormalities, such as decreased hepatic or muscular glycogen storage and reduced oxygen consumption during activity [25]. Furthermore, muscle weakness in the distal (ankle plantar and dorsiflexors) and proximal (knee extensors and flexors) muscles of the lower extremities, as well as muscle size reduction in the proximal muscles of the lower extremity as a result of DPN [26], could explain the significant increase in fatigability among patients with T2DMPN. T2DMPN causes increased muscle fatigability, which can affect various muscular groups in the lower limb during both isometric and dynamic tasks [18].Furthermore, increased accumulation of intramuscular non-contractile tissue within muscular tissue due to neuropathy has been linked to decrease muscle strength in the calf and thigh muscles among patients with DPN [27], which is another possible explanation for increased fatigue in patients with T2DMPN. This could explain why patients with T2DMPN had a substantial influence on the physical component of QoL in the current study. Fatigue has also been noted as an impediment to diabetes patients' daily self-care management [24]. The mechanisms underlying the increased muscle fatigue associated with diabetes are unknown [18]. It has been suggested that this diabetes complication is linked to a failure of neuromuscular transmission.

Secondly, the current research found that T2DM had no effect on social health. This could imply that some T2DM or T2DMPN patients can cope socially with the disease's challenges. This is substantiated by the fact that the typical large size of Arab communities and the inherent close proximity of extended family are always associated with stronger social support; and the favorable relationship between social support and general health is widely documented [28]. Furthermore, glycemic management has been shown to improve psychological well-being in T2DM patients [29]. Furthermore, people with T2DM are well-known for being active and capable of self-care within their sociocultural background [29]. Social support perceptions may be influenced by race and ethnicity, as well as sociodemographic and sociocultural determinants [29]. As a result, more research is needed to understand more about the influence of T2DM on social dimension of QoL. Financial status, education level, family support, efficient healthcare management and follow-up, sociocultural and home care services are all factors that may have an impact on the social components of QoL in patients with T2DM and should be thoroughly investigated. Physical and social components of QoL are related through racial disparities, socioeconomic determinants, the built environment, and clinical issues [30, 31]. As a result, it's conceivable that interventions for patients with T2DM should be tailored to particular race or ethnicity in order to improve QoL.

The most important, independent risk factors for T2DM-associated DPN, according to a recent review of T2DM patients with DPN from 14 countries, were duration of diabetes, poor glycemic control, history of hypertension, cardiovascular disease, and depressive symptoms [32]. Depressive symptoms have been have been identified as a significant risk factor for patients with T2DMPN. The study's claimed 14 countries, however, did not include any Arab nations. As a result, our findings on QoL, particularly the relevance of PCS and MCS components, will have considerable implications for the development of T2DM healthcare and therapy in Saudi Arabia. Prior to health management and policymaking, it is recommended that each territory recognize the functioning of physical and psychosocial components of QoL.

This is also the only study we are aware of that looked into the relationship between fatigue and QoL in Saudi Arabian diabetics. Several limitations, however, limit the interpretation of our findings. For example, the majority of data was self-reported, which could lead to under- or over-reporting of medical problems, complications, and comorbidities. Although current evidence is not fully understood, it has been suggested that these changes in PCs and MCS in QoL T2DMPN may be due to possible neurovascular damage in musculoskeletal components. As a result, more research is needed to identify the relevent factors that influence QoL in T2DM patients.

Conclusion

T2DM with DPN has a significant impact on fatigability and physical aspects of QoL. This could be because of T2DM's pathological and diabetic management repercussions. The findings suggest that further efforts are needed to improve or maintain physical performance and QoL in T2DMPN patients.

Declarations

Ethics approval and consent to participate:

All methods were performed in accordance with relevant regulations and guidelines. Each participant signed an informed consent form and received a detailed description of the study procedure prior to the start of the evaluation. The Research and Ethics Committee of King Saud University's College of Applied Medical Sciences approved this study, approval no: E-19-3731.

Consent for publication:

Not Applicable

Availability of data and materials:

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors declare no competing interests.

Funding:

No funding received for this study

Authors' contributions:

1. Muneera Almurdi: Concept & Review of Literatures

2. Asma Alrashoud: Concept & Review of Literatures

3. Reema Alhamdan: Subject identification & Data collection

4. Norah Alammar: Subject identification &Data collection

5. Ghaidaa Alshehri: Subject identification &Data collection

6. Maha Rifaey: Subject identification & Data collection

7. Muneera Alsaleh: Manuscript Preparation

8. Shaji John Kachanathu: Manuscript Preparation and submission

9. Sami AlAbdulwahab: Statistical & Result Analysis

Acknowledgements:

The authors would like to express their appreciation to the Deanship of Scientific Research, Research Center, College of Applied Medical Sciences and RSSU at King Saud University for their constructive scientific and technical support during this research.

References

1. World Health Organization. Diabetes: Fact Sheet. Available online: https://www.who.int/news-room/fact-sheets/detail/diabetes (accessed on 30 July 2021).
2. Federation, I. D. (2017). IDF diabetes atlas 8th edition. International Diabetes Federation, 905-911.
3. Alwin Robert, A., Abdulaziz Al Dawish, M., Braham, R., Ali Musallam, M., Abdullah Al Hayek, A., & Hazza Al Kahtany, N. (2017). Type 2 diabetes mellitus in Saudi Arabia: major challenges and possible solutions. Current diabetes reviews, 13(1), 59-64.
4. Al Mansour, M. A. (2020). The prevalence and risk factors of type 2 diabetes mellitus (DMT2) in a semi-urban Saudi population. International journal of environmental research and public health, 17(1), 7.

5. Wang, D. D., Bakhotmah, B. A., Hu, F. B., & Alzahrani, H. A. (2014). Prevalence and correlates of diabetic peripheral neuropathy in a Saudi Arabic population: a cross-sectional study. PloS one, 9(9), e106935.
6. Bahhary, M., Alkhaldi, Y. M., & Alsaleem, S. A. (2021). Awareness regarding diabetic peripheral neuropathy and its risk factors among diabetics in Muhayil City, Saudi Arabia. Middle East Journal of Family Medicine, 7(10), 113.
7. Schmidt-RioValle, J., Abu Ejheisheh, M., Membrive-Jiménez, M. J., Suleiman-Martos, N., Albendín-García, L., Correa-Rodríguez, M., & Gómez-Urquiza, J. L. (2020). Quality of Life After Coronary Artery Bypass Surgery: A Systematic Review and Meta-Analysis. International Journal of Environmental Research and Public Health, 17(22), 8439.
8. Vu, G. T., Tran, B. X., Hoang, C. L., Hall, B. J., Phan, H. T., Ha, G. H., ... & Ho, R. (2020). Global research on quality of life of patients with HIV/AIDS: is it socio-culturally addressed? (GAPRESEARCH). International journal of environmental research and public health, 17(6), 2127.
9. Van der Vinne, E. (2009). The ultimate goal of disease management: improved quality of life by patient centric care. International journal of integrated care, 9.
10. Kalra, S., & Sahay, R. (2018). Diabetes fatigue syndrome. Diabetes Ther, 9, 1421–1429.
11. Bi, Y. X., Zhang, L., Li, X. N., Kan, Y. S., Li, S., Zou, Y., ... & Zhang, Y. (2021). Contributing factors of fatigue in patients with type 2 diabetes: A systematic review. Psychoneuroendocrinology, 105280.
12. Orlando, G., Balducci, S., Bazzucchi, I., Pugliese, G., & Sacchetti, M. (2017). Muscle fatigability in type 2 diabetes. Diabetes/metabolism research and reviews, 33(1), e2821.
13. Valko, P. O., Bassetti, C. L., Bloch, K. E., Held, U., & Baumann, C. R. (2008). Validation of the fatigue severity scale in a Swiss cohort. Sleep, 31(11), 1601-1607.
14. Ware Jr, J. E. (2000). SF-36 health survey update. Spine, 25(24), 3130-3139.
15. Meyer-Rosberg, K., Burckhardt, C. S., Huizar, K., Kvarnström, A., Nordfors, L. O., & Kristofferson, A. (2001). A comparison of the SF-36 and Nottingham Health Profile in patients with chronic neuropathic pain. European journal of pain, 5(4), 391-403.
16. Young, M. J., Boulton, A. J. M., MacLeod, A. F., Williams, D. R. R., & Sonksen, P. H. (1993). A multicentre study of the prevalence of diabetic peripheral neuropathy in the United Kingdom hospital clinic population. Diabetologia, 36(2), 150-154.
17. Callaghan, B. C., Cheng, H. T., Stables, C. L., Smith, A. L., & Feldman, E. L. (2012). Diabetic neuropathy: clinical manifestations and current treatments. The lancet NEUROLOGY, 11(6), 521-534.
18. Orlando, G., Sacchetti, M., D'Errico, V., Haxhi, J., Rapisarda, G., Pugliese, G., & Balducci, S. (2020). Muscle fatigability in patients with type 2 diabetes: relation with long-term complications. Diabetes/Metabolism Research and Reviews, 36(2), e3231.
19. Alabdulwahab, S., & Muneera, A. M. (2010) Whirlpool Therapy Improves Nerve Function and Dynamic Standing Balance in Patients with Diabetic Peripheral Neuropathy. Journal of Physical Medicine and Rehabilitation Sciences, 13,58-64

20. Almurdhi, M. M., Brown, S. J., Bowling, F. L., Boulton, A. J. M., Jeziorska, M., Malik, R. A., & Reeves, N. D. (2017). Altered walking strategy and increased unsteadiness in participants with impaired glucose tolerance and Type 2 diabetes relates to small-fibre neuropathy but not vitamin D deficiency. Diabetic medicine, 34(6), 839-845.
21. Nguyen, H. V., Tran, T. T., Nguyen, C. T., Tran, T. H., Tran, B. X., Latkin, C. A., ... & Ho, R. (2019). Impact of comorbid chronic conditions to quality of life among elderly patients with diabetes mellitus in Vietnam. International journal of environmental research and public health, 16(4), 531.
22. Donald, M., Dower, J., Coll, J. R., Baker, P., Mukandi, B., & Doi, S. A. (2013). Mental health issues decrease diabetes-specific quality of life independent of glycaemic control and complications: findings from Australia's living with diabetes cohort study. Health and quality of life outcomes, 11(1), 1-8.
23. Martino, G., Catalano, A., Bellone, F., Russo, G. T., Vicario, C. M., Lasco, A., ... & Morabito, N. (2019). As time goes by: anxiety negatively affects the perceived quality of life in patients with type 2 diabetes of long duration. Frontiers in psychology, 10, 1779.
24. Griggs, S., & Morris, N. S. (2018). Fatigue among adults with type 1 diabetes mellitus and implications for self-management: An integrative review. The Diabetes Educator, 44(4), 325-339.
25. Fritschi, C., & Quinn, L. (2010). Fatigue in patients with diabetes: a review. Journal of psychosomatic research, 69(1), 33-41.
26. Almurdhi, M. M., Reeves, N. D., Bowling, F. L., Boulton, A. J., Jeziorska, M., & Malik, R. A. (2016). Reduced lower-limb muscle strength and volume in patients with type 2 diabetes in relation to neuropathy, intramuscular fat, and vitamin D levels. Diabetes Care, 39(3), 441-447.
27. Tuttle, L. J., Sinacore, D. R., Cade, W. T., & Mueller, M. J. (2011). Lower physical activity is associated with higher intermuscular adipose tissue in people with type 2 diabetes and peripheral neuropathy. Physical therapy, 91(6), 923-930.
28. Romano-Zelekha, O., Golan, E., Ifrah, A., Weinstein, T., & Shohat, T. (2017). Differences in quality of life between Jewish and Arab patients on hemodialysis. Quality of Life Research, 26(12), 3343-3352.
29. Song, Y., Nam, S., Park, S., Shin, I. S., & Ku, B. J. (2017). The impact of social support on self-care of patients with diabetes: What is the effect of diabetes type? Systematic review and meta-analysis. The Diabetes Educator, 43(4), 396-412.
30. Babazadeh, T., Dianatinasab, M., Daemi, A., Nikbakht, H. A., Moradi, F., & Ghaffari-Fam, S. (2017). Association of self-care behaviors and quality of life among patients with type 2 diabetes mellitus: Chaldoran County, Iran. Diabetes & metabolism journal, 41(6), 449-456.
31. Olukotun, O., Akinboboye, O., Williams, J. S., Ozieh, M., & Egede, L. E. (2021). Influences of Demographic, Social Determinants, Clinical, Knowledge, and Self-Care Factors on Quality of Life in Adults with Type 2 Diabetes: Black-White Differences. Journal of Racial and Ethnic Health Disparities, 1-12.
32. Lu, Y., Xing, P., Cai, X., Luo, D., Li, R., Lloyd, C., ... & Li, M. (2020). Prevalence and risk factors for diabetic peripheral neuropathy in type 2 diabetic patients from 14 countries: estimates of the

INTERPRET-DD study. Frontiers in public health, 8.