Screening for Depressive Symptoms amongst Patients with Diabetic Peripheral Neuropathy

Rahab Marhoon Alghafri, Alfred Gatt, Cynthia Formosa

Faculty of Health Sciences, University of Malta.
Address correspondence to: Cynthia Formosa, e-mail: cynthia.formosa@um.edu.mt

Manuscript submitted September 13, 2020; accepted September 30, 2020

Abstract

AIM: The study aimed to determine if there is a relationship between having diabetic peripheral neuropathy and the development of depressive symptoms in patients with type 2 diabetes mellitus (T2DM). RESEARCH DESIGN AND METHOD: A comparative non-experimental study was conducted. Ninety-five T2DM individuals aged 65 years and more were recruited. The sample was divided into two groups: 50 participants with T2DM only and 45 participants with DPN. The Patient Health Questionnaire-9 (PHQ-9) was used to collect information about low mood/depression symptoms in the recruited subjects. RESULTS: Participants with DPN recorded higher scores of PHQ-9 than those with T2DM only. The mean PHQ 9 score for the Diabetic Peripheral Neuropathy group (6.09) was significantly higher than the mean PHQ 9 score for the T2DM group (2.24) (p<0.001). Participants with DPN were more likely to have a mild/moderate or moderately severe low mood/depression symptoms, when compared to Type 2 DM participants who exhibited minimal to no low mood/depressive symptoms. CONCLUSION: The association between diabetic neuropathy and depression is confirmed, with significant depressive symptoms found in patients with neuropathy when compared to patients with diabetes with no complications. Therefore, complaints caused by DPN and emotional problems associated with DPN should be addressed in the management of DPN in order to prevent depressive symptoms. A call for change in screening practices to help identify patients with DM and depressive symptoms is warranted.

Keywords: diabetes · diabetic foot · peripheral neuropathy · depression · T2DM · screening · type 2 diabetes

1. Introduction

Depression and diabetes have surely ranked amongst the defining epidemics of the 21st century, given the current explosion in the prevalence rates of both these conditions in the world [1]. The high prevalence rate of both diabetes and depression is well established, therefore it is not surprising that these two conditions could interact when both are present, leading to additional morbidity and a higher mortality risk in patients living with diabetes. Despite this, the specific relationship between depression and DPN remains unclear. Furthermore, neuropathic pain may deteriorate the general health status of patients with diabetes [2]. The most common mood disorder is low mood leading to depression, which is one of the mental disorders, that can be found in patients with diabetes [3]. Low mood/depression is defined as having signs of sadness, feeling of anxiety or panic, worry, low self-esteem, tiredness, anger, frustration, thoughts about death, losing or gaining weight and alteration in activity and sleep pattern for more than two weeks. Depressed individuals practice at least four of the fore-mentioned signs and symptoms [4]. Depression is classified as a very common and serious medical condition [5].

Diabetes itself can aggravate the symptoms of depression and depression increases the risk of aggravating Type 2 diabetes mellitus [6]. This is due to the link between depression and poor controlled health behaviors such as low physical activities, smoking, high food consumption which are directly linked to obesity and poor glucose control [7]. The association between depression and chronic conditions has
been confirmed by several studies [8], leading to low quality of life [9]. Although, many studies indicated the association between poor or low control of diabetes and depression, this still is not given the appropriate attention as other chronic health conditions [10]. Thus, this study sought to determine the association between diabetic peripheral neuropathy and depressive symptoms by measuring low mood symptoms in participants with type 2 diabetes mellitus and comparing results to the low mood symptoms in participants with diabetic peripheral neuropathy.

2. Methods

2.1 Study design

We performed a non-experimental, comparative quantitative study in a diabetes primary care setting. The University of Malta Research Ethics Committee approved this study and after obtaining informed consent participants living with T2DM were categorized into 2 groups using convenience sampling. Patients who satisfied the following inclusion criteria were recruited as follows: Group 1 - 50 participants with T2DM only and Group 2 - 45 participants with DPN. The following inclusion criteria were designed for the study: Male and female participants aged 60 years or more. 50 participants diagnosed with type 2 diabetes mellitus and 45 participants diagnosed with diabetic peripheral neuropathy. Participants had to show willingness to sign informed consent and participate in the study. Participants were excluded from the study if they presented with Type 1 diabetes. Having other comorbidities that are chronic in nature such as Peripheral Vascular Disease (PVD), Spinal Canal Stenosis and Arthritis. A history of foot ulceration and were on anti-depressant medications during the time of the study. The participants who agreed to participate were interviewed once during the study. Demographic data including gender, age, level of education, medications and their latest HbA1c level were recorded. The participants were asked to respond to the questions of the Patient Health Questionnaire 9 (PHQ-9) [11].

2.2 Diabetic peripheral neuropathy

Prior to the start of the interview, participants were assessed for peripheral neuropathy symptoms by a state registered podiatrist using the 10-g monofilament and the 128HZ tuning fork. Participants with a positive test for neuropathy results were included in Group 2. Neurological assessment was performed in a quiet room by the same investigator to ensure repeatability.

The first tool used in this study was the 128Hz tuning fork. This was applied first by striking the tuning fork so that it vibrated appropriately without creating audible humming. The tuning fork was then placed on the medial border of the hallux after the patient was instructed to close his eyes. The participant was instructed to inform the practitioner on the type of sensation perceived. The participant was instructed to also inform the practitioner exactly when the vibrating sensation ceased. The examiner certified the absence of vibration at once, by placing the tuning fork on the dorsal aspect of the bony prominence of his or her own thumb. Normally, the practitioner is able to feel the vibration persist for at least 10 seconds after the participant, this was considered to be normal. The test was performed on both feet. For a diagnosis of neuropathy, the patient had to be unable to feel a buzzing sensation when the vibrating tuning fork was applied and at the same time pinpoint the moment that the tuning fork stopped vibrating. The patients who managed to satisfy these criteria were given the score ‘absent’. If the patient was able to feel the vibrating stimulus on the hallux then the patient was given a score of ‘present’.

The 10-g Semmes–Weinstein monofilament was used to identify peripheral sensory neuropathy as previously described by Boulton [12]. The 5-point test was used. The plantar aspect of the hallux and third digit together with the first, third, and fifth metatarsal heads were used for testing. With the eyes closed, the patient related to the investigator when he or she could feel the monofilament. Inability to feel the 10-g of pressure was considered to be indicative of peripheral neuropathy.

2.3 Study tool for the measurement of low mood / depression

The early detection of low mood symptoms is important to prevent further complications such as depression, since the literature suggests that low mood lasting for two weeks or more is a symptom of depression [13]. There are several scales used to test for depression including the Hospital Anxiety and depression Scales (HADS) [14], The Patient Health Questionnaire 2 (PHQ-2) [11], and The Patient Health Questionnaire 9 (PHQ-9) [15] amongst others.
For the purpose of this study the Patient Health Questionnaire-9 (PHQ-9) was utilized to collect the information about low mood/depression symptoms in the recruited subjects. The PHQ-9 is an easy self-rating tool that can be used alone or after using the PHQ-2 questionnaire to assess low mood/depressive symptoms [11]. It has been validated to be used clinically [15] and has a sensitivity rate of 61% and specificity of 94% in adults and requires no permission from the authors to be used in the clinical setting [11]. It can be used to make a tentative diagnosis of depression in at-risk populations, such as those patients with coronary heart disease or those following stroke. This tool has been validated for use in primary care settings [16]. Validity has been assessed against an independent structured mental health professional (MHP) interview. PHQ-9 score ≥10 had a sensitivity of 88% and a specificity of 88% for major depression [11]. It can even be used over the telephone [17]. Studies found the PHQ-9 is also useful for screening for depression in psychiatric clinics [18].

It consists of 9 questions with four answer options. The first option is “not at all” scored as 0, the second option is “several days” with a score of 1, the third option is “more than half days” with a score of 2 and the fourth option is “nearly every day” with a score of 3. The participants are select requested to select one of the four response options for each of the 9 questions. The final PHQ-9 score indicates the severity of low mood/depression [11]. The interpretation of the total score of the PHQ-9 is classified into five subgroups. The minimum score can be recorded is (0) and the maximum score is (27). The PHQ-9 classification groups are classified as following.

- Score 1-4 Minimal depression
- Score 5-9 Mild depression
- Score 10-14 Moderate depression
- Score 15-19 Moderately severe depression
- Score 20-27 Severe depression

The results of the PHQ-9 may be used to make a depression diagnosis according to DSM-IV criteria and takes less than 3 minutes to complete. The total of all 9 responses from the PHQ-9 aims to predict the presence and severity of depression. Primary care providers use the PHQ-9 to screen for depression in patients. A provisional diagnosis of Major Depressive Disorder can be made by using responses to PHQ-9 questions to fulfill the diagnostic criteria of DSM-5. According to DSM-5, Major Depressive Disorder is likely if 5 or more of the 9 symptoms are present for “most of the day, nearly every day” in the past 2 weeks and one of the symptoms is depressed mood or little interest or pleasure in doing things (questions 1 and 2 on the PHQ-9). Any degree of suicidal thoughts counts toward this criteria. The symptoms must also cause significant distress and loss of function, and the symptoms must not be better explained by substance use or another medical or psychiatric condition. “Other” depression is diagnosed if there is significant impairment and/or distress in major areas of functioning, but the full criteria for any specific depressive disorder are not met. Clinicians may also use the PHQ-9 to evaluate treatments given for depression. A change of PHQ-9 scores to less than 10 is considered a "partial response" to treatment and a change of PHQ-9 score to less than 5 is considered to be “remission.” [19].

2.4 Statistical analysis

All data were recorded on a spreadsheet designed in Microsoft Excel to group together the information required for interpretation of the results. Results Data are expressed as mean ± standard deviation. Descriptive statistics were used to characterize clinical variables of the studied patients. This data was analyzed by utilizing the IBM SPSS (Statistical Package for Social Sciences) program. The overall scores of low mood/depression symptoms and descriptive analysis were carried out on the main study variables between both participants groups. Mean values of gender, age, level of education, treatment of diabetes, other medication taken, presence of neuropathy, HbA1c levels, duration of having neuropathy were recorded. The Shapiro Wilk test was used to test normality distribution of PHQ-9 scores for both groups. The non-parametric Mann Whitney test was used to compare mean PHQ 9 scores between the two groups since data was not normally distributed. The Chi Square test was used to investigate the association between the PHQ 9 score classification (None or minimal, Mild, Moderate, Moderately severe depression) and Group (Diabetes Type 2, Diabetic Peripheral Neuropathy).

3. Results

A total of 95 participants, 52 males and 43 females were recruited in this study. The number of participants with Type 2 Diabetes only and participants with Diabetic Peripheral Neuropathy (DPN) were 50 and 45 respectively. The mean age of the
The study population was 77.55 yrs (SD. 6.212). Most of the participants reported having Secondary level education (n=50). Whilst only a few participants reported having tertiary level of education (n=4). The mean HbA1c for the Group 1 was reported at 5.9% (SD 0.85) whilst the mean HbA1c for Group 2 was 8.2% (SD 1.74). The mean duration of neuropathy for Group 2 was 5.9 years (SD 4.04).

3.1 Individual responses to the PHQ-9 questionnaire

Tables 1 and 2 below include individual responses of the PHQ-9 questionnaire for both study groups. It is evident from the percentages reported that the participants with peripheral neuropathy demonstrated more depressive symptoms than the participants with DM only.

3.2 Difference in mean PHQ-9 scores between the study groups

The mean PHQ 9 score for the Diabetic Peripheral Neuropathy group (6.09) was significantly higher than the mean PHQ 9 score for the T2DM group (2.24) (p<0.001). Table 3 below demonstrates the statistical difference in the mean PHQ-9 scores between the study groups.

3.3 Measuring the strength of the association

The Chi Square test was used to investigate the association between the PHQ 9 score classification (None or minimal, Mild, Moderate, Moderately severe) and Groups (T2DM VS DPN). Participants Group 1 were found to likely have a minimal to none low mood/depression symptoms than their counterparts in Group 2. On the other hand, participants in the Diabetic Peripheral Neuropathy group were more likely to have a mild/moderate or moderately severe low mood/depression symptoms than their counterparts in the Diabetes Type 2 group. $X^2(3) = 18.729, p < 0.001$ (Table 4, Figure 1).

Figure 1: Percentages of Patient health questionnaire-9 (PHQ-9) scores classifications for each group.

4. Discussion

Based on our data, this study has demonstrated that depression and anxiety disorders exist more frequently in patients with diabetes and DPN. In this article we aim to alert clinicians to the fact that low mood and depression are common in patients with diabetes presenting with DPN and that these conditions can complicate matters and impair positive outcomes if both are overlooked and

Table 1: Responses for the Participants with Type 2 Diabetes Mellitus only. (N= 50)

| Questions PHQ-9                                                                 | Not at all | Several days | More than half the days | Nearly every day |
|--------------------------------------------------------------------------------|------------|--------------|-------------------------|-----------------|
| Little interest or pleasure in doing things.                                  | 82%        | 14%          | 2%                      | 2%              |
| Feeling down, depressed, or hopeless.                                         | 84%        | 12%          | 4%                      | 0%              |
| Trouble falling or staying asleep, or sleeping too much.                      | 68%        | 20%          | 4%                      | 8%              |
| Feeling tired or having little energy.                                         | 58%        | 32%          | 10%                     | 0%              |
| Poor appetite or over eating.                                                 | 80%        | 12%          | 8%                      | 0%              |
| Feeling bad about yourself or your family.                                    | 92%        | 6%           | 2%                      | 0%              |
| Trouble concentrating on things, such as reading the newspaper or watching TV.| 96%        | 2%           | 2%                      | 0%              |
| Moving or speaking so lowly that other people could have noticed? Or the opposite. | 84%        | 12%          | 2%                      | 2%              |
| Thoughts that you would be better off dead or hurting yourself in some way     | 98%        | 0%           | 2%                      | 0%              |
not addressed simultaneously in the clinical scenario. Therefore, complaints caused by DPN and emotional problems associated with DPN should be addressed in a timely manner in the management of diabetes and DPN in order to prevent severe depressive symptoms in these patients. Depression is a growing concern in the 21st century and according to the World Health Organization, unipolar depressive disorders were ranked as the third leading cause of the global burden of disease in 2004 and will move into the first place by 2030 [20].

Depressive symptoms need to be given its rightful importance especially amongst the high-risk population with many co-morbidities such as diabetes. Thus the authors recommend routine screening for depression and anxiety in patients presenting with DPN, which to date is not standard practice amongst healthcare professionals at both primary and secondary care [21], even though the American Diabetes Association has recommended that patients with DM, especially patients with poorly controlled blood glucose, should be screened for

### Table 2: Responses for the Participants with Diabetes peripheral neuropathy. (N= 45)

| Questions PHQ-9                                                                 | Not at all | Several days | More than half the days | Nearly every day |
|---------------------------------------------------------------------------------|------------|--------------|-------------------------|------------------|
| 1. Little interest or pleasure in doing things.                                 | 55.55%     | 17.77%       | 11.11%                  | 15.55%           |
| 2. Feeling down, depressed, or hopeless.                                        | 53.33%     | 20%          | 17.77%                  | 8.88%            |
| 3. Trouble falling or staying asleep, or sleeping too much.                     | 46.66%     | 26.66%       | 15.55%                  | 11.11%           |
| 4. Feeling tired or having little energy.                                       | 40%        | 24.44%       | 13.33%                  | 22.22%           |
| 5. Poor appetite or over eating.                                                | 42.22%     | 24.44%       | 24.44%                  | 8.88%            |
| 6. Feeling bad about yourself or your family.                                   | 66.66%     | 20%          | 11.11%                  | 2.22%            |
| 7. Trouble concentrating on things, such as reading the newspaper or watching TV | 80%        | 11.11%       | 6.66%                   | 2.22%            |
| 8. Moving or speaking so slowly that other people could have noticed? Or the opposite | 77.77%     | 11.11%       | 8.88%                   | 2.22%            |

### Table 3: The Mann Whitney test - Difference in PHQ-9 scores between the study group

| Group Number and Description | Sample Size | Mean PHQ 9 | Std. Deviation | P-value |
|------------------------------|-------------|------------|----------------|---------|
| Group 1 - Participants with T2DM | 50          | 2.24       | 2.631          | 0.000   |
| Group 2 - Participants with DPN  | 45          | 6.09       | 4.804          |         |

### Table 4: Percentages of Patient health questionnaire-9 (PHQ-9) scores classifications for each group. (X²(3) = 18.729, p < 0.001)

| PHQ 9 Score Classifications | Group with T2DM | Group with DPN | Total |
|------------------------------|-----------------|----------------|-------|
| Minimal or None              | Count           | Count          | Total |
|                              | Percentage      | Percentage     |       |
| Mild                         | Count           | Count          | Count |
|                              | Percentage      | Percentage     |       |
| Moderate                     | Count           | Count          | Count |
|                              | Percentage      | Percentage     |       |
| Moderately Severe            | Count           | Count          | Count |
|                              | Percentage      | Percentage     |       |
depression [22] Thus, a call for change in screening practices for patients with DM is warranted.

Healthcare professionals should be familiarized with PHQ-9 Health Questionnaire and other similar screening questionnaires and to use them routinely in their practice adjunct to the normal consultation. These questionnaires are not time consuming, efficient, and reliable tools to detect patients with depressive disorders. If low mood or depressive symptoms are detected, a prompt treatment plan should be implemented including nonpharmacologic and/or pharmacologic options and prompt referral to appropriate healthcare professionals.

4.1 Limitations of the study

The study sample size was limited to 95 participants since it was difficult to find participants with DPN without having history of previous ulcer or without having a current ulcer or no other diabetes-related complications such as Peripheral arterial disease. Having a larger number of participants could have given more strength to the results of this study. Thus, it is greatly recommended that this study will be repeated in larger population in view that mental health issues are currently reported to be one of the major global health issues. The modalities used in this study to diagnose DPN may not be so sensitive to detect early neuropathy and small-fibre impairment thus patients with rather advanced neuropathy could have been included in this study. However, the 10-g monofilament and the 128HZ tuning fork are the standard clinical tools used in primary care clinics to diagnose DPN.

Patient compliance in answering the questions of the PHQ-9 Health Questionnaire could also have posed a limitation to the study findings. Since the questionnaire relies on patient self-report, all responses should be verified by the clinician, and a definitive diagnosis is made on clinical grounds taking into account how well the patient understood the questionnaire, as well as other relevant information from the patient. For instance, participants found it difficult to score question 9 which stated that “Thoughts that you would be better off dead, or of hurting yourself” since some patients found it hard to express or estimate their feelings to give a correct score. To overcome this difficulty participants were given further explanation and examples for each question to understand better the question being imposed.

5. Conclusion

Depression seems to be a frequent co-morbid condition in diabetic patients with DPN. Thus, patients with neuropathic symptoms caused by neuropathy are at a high risk for depression. Therefore, complaints caused by DPN and emotional problems associated with DPN should be addressed in the management of DPN in order to prevent depressive symptoms in patients with diabetes. Finally, we recommend a more widespread dissemination of this information through continuing medical education programs and other relevant means to improve outcomes in this population. More studies are needed to test the usefulness of the screening for depressive disorders amongst T2DM patient with DPN.

6. Acknowledgements

The authors would like to thank all participants who consented to participate in this study.

7. Declaration of interest

The authors report no conflict of interest

References

1. Jain R, Jain S, Raison CL, Maletic V. Painful Diabetic Neuropathy is More than Pain Alone: Examining the Role of Anxiety and Depression as Mediators and Complicators. Curr Diab Rep 2011. 11:275-284.
2. Vas PRJ, Papanas N. Depression and Diabetic Peripheral Neuropathy: Birds of a Feather, But When do They Flock Together? Exp Clin Endocrinol Diabetes 2020. 128(05):347-349.
3. Vileikyte L, Leventhal H, Gonzalez J, et al. Diabetic peripheral neuropathy and depression symptoms: the association revisited. Diabetes Care 2005. 28:2378-2383.
4. Cooper R. Diagnosing the Diagnostic and Statistical Manual of Mental Disorders (5th ed.). New York: Routledge. 2018.
5. Bromet E, Andrade L, Hwang I, Sampson N, Alonso J, de Girolamo G, de Graaf R, Demyttenaere K, Hu C, Iwata N, Karam AN, Kaur J, Kostyuchenko S, Lépine JP, Levinson D, Matschinger H, Mora MEM, Browne MO, Posada-Villa J, Viana MC, Williams DR, Kessler RC. Cross-national epidemiology of DSM-IV major depressive episode. BMC Medicine 2011. 9(1):90.
6. Mezuk B, Eaton W, Albrecht S, Golden S. Depression and Type 2 Diabetes Over the Lifespan: A meta-analysis. Diabetes Care 2008. 31(12):2383-2390.
7. Strine T, Mokdad A, Dube S, Balluz L, Gonzalez O,
Berry J, Mandscheid R, Kroenke K. The association of depression and anxiety with obesity and unhealthy behaviors among community-dwelling US adults. Gen Hosp Psychiatry 2008. 30(2):127-137.

8. McGrath N, McHugh S, Kearney PM, Toomey E. Barriers and enablers to screening and diagnosing depression and diabetes distress in people with type 2 diabetes mellitus; protocol of a qualitative evidence synthesis. HRB Open Res 2020. 2:26.

9. Cassano P, Fava M. Depression and public health: an overview. J Psychosom Res 2002. 53(4):849-857.

10. Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. Lancet 2007. 370(9590):851-858.

11. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001. 16(9):606-613.

12. IWGDF Guidelines. Available from: https://iwgdf-guidelines.org/guidelines/guidelines; 2019.

13. Lustman P, Clouse R. Depression in diabetic patients. The relationship between mood and glycemic control. J Diabetes Complications 2005. 19(2):113-122.

14. Djukanovic I, Carlsson J, Årestedt K. Is the Hospital Anxiety and Depression Scale (HADS) a valid measure in a general population 65–80 years old? A psychometric evaluation study. Health Qual Life Outcomes 2017. 15(1):193.

15. Cameron IM, Crawford JR, Lawton K, Reid IC. Psychometric comparison of PHQ-9 and HADS for measuring depression severity in primary care. Br J Gen Pract 2008. 58(546):32-36.

16. Haddad M, Walters P, Phillips R, Tsakok J, Williams P, Mann A, Tylee A. Detecting depression in patients with coronary heart disease: a diagnostic evaluation of the PHQ-9 and HADS-D in primary care, findings from the UPBEAT-UK study. PLoS One 2013. 8(10):e78493.

17. Pinto-Meza A, Serrano-Blanco A, Penarrubia MT, Blanco E, Haro JM. Assessing depression in primary care with the PHQ-9: can it be carried out over the telephone? J Gen Intern Med 2005. 20(8):738-742.

18. Inoue T, Tanaka T, Nakagawa S, Nakato Y, Kameyama R, Boku S, Toda H, Kurita T, Koyama T. Utility and Limitations of PHQ-9 in a Clinic Specializing in Psychiatric Care. BMC Psychiatry 2012. 12:73.

19. Kroenke K, Spitzer RL. The PHQ-9: A New Depression Diagnostic and Severity Measure. Psychiatric Annals 2002. 32(9):1-7.

20. World Health Organization. Depression. 2020. Available online: https://www.who.int/news-room/fact-sheets/detail/depression

21. Katon W, Lin E, Williams L, Ciechanowski P, Heckbert S, Ludman E, Rutter C, Crane PK, Oliver M, Korff MV. Comorbid Depression Is Associated with an Increased Risk of Dementia Diagnosis in Patients with Diabetes: A Prospective Cohort Study. J Gen Intern Med 2010. 25(5):423–429.

22. Standards of Medical Care in Diabetes. Diabetes Care 2004. 28(Supp 1):S4-S36.