Depression, Anxiety and Sexual Dysfunction in Patients with Diabetes Mellitus With and Without Foot Ulcer

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ABSTRACT

Introduction: Anxiety and depression are both associated with increased morbidity in diabetic population, especially those afflicted with foot ulcer, whereas Erectile Dysfunction (*"ED"*) and Female Sexual Dysfunction (*"FSD"*) are amongst the common complication found in diabetes. This study aimed to determine the prevalence of anxiety and depression as primary outcome and sexual dysfunction (*"SD"*) as a secondary outcome in diabetic patients with and without foot ulcer (*"DFU"*). **Methods:** A cross-sectional study was conducted in Hospital Raja Permaisuri Bainun Ipoh, Perak, where 164 diabetic patients were recruited for the purpose of this study. *Hospital Anxiety and Depression Scale* ("HADS") were utilised to measure anxiety and depression. *International Index for Erectile Function 5* ("IIEF-5") and the Malay version of *Female Sexual Function Index* ("MVFSFI") were used to detect *SD*. Simple and multiple logistic regressions were referred to in order to evaluate the factors associated with anxiety, depression and *SD*. **Results:** In the group with foot ulcer, 36.8% had depressive and anxiety risk respectively compared to without the foot ulcer, 37.5% and 38.5% respectively. Male gender (AOR=6.3,p=0.002,95%CI 1.975, 20.205) and having lower education status (AOR=6.0,p=0.018,95%CI1.36,26.59,) was associated with foot ulcer. High prevalence of *SD* found in foot ulcer group (52.6%,p=0.006). Those with depression (OR=4.421,95% CI 1.08,18.16,p=0.039) and male gender (OR=18.42,p<0.01,95%CI5.5,-61.62) predicts present of *SD*. **Conclusion:** Depression and anxiety prevalent were similar for both with and without diabetic foot ulcer. Several significant predictor factors were identified for *DFU* group, for anxiety and depression risk and for *SD* in a diabetes patient. Further studies are required to establish the directional nature of this relationship.

Keywords: Depression, Anxiety, Diabetic food ulcer (*DFU*), Erectile Dysfunction (*ED*), Female Sexual Dysfunction (*FSD*)

INTRODUCTION

Diabetes Mellitus (*"DM"*) is a metabolism disorder which leads to inappropriate hyperglycaemia either due to a reduction in the biologic effectiveness of insulin or an absolute deficiency of insulin secretion, or both. In Malaysia, the prevalence of diabetes has increased in the last decade from 11.6% in 2006 to 15.2% in 2011 to 17.5% (3.5 million) in 2015 among individuals 18 years and above.[1] In general, Type 2 *DM* may result in various complications namely nephropathy, retinopathy, neuropathy and dermatopathy.[2] About 60% of diabetic foot ulcers are the result of underlying neuropathy[3] and vasculopathy, which retards the healing process.[2] Diabetic foot ulcer (*"DFU"*) is an open wound commonly located on the foot that occurs in about 15% of patient with diabetes and approximately 4.3% had lower limb amputation.[2]

Depression and anxiety may affect body metabolism in various ways. Studies showed stressful emotional experiences affect hormones release that may counter the insulin action (i.e. catecholamines, glucocorticoids, growth hormone and glucagons) and affect blood glucose level both in normal people and people with *DM*. Metaanalysis study showed depression was a risk factor for developing type 2 DM, where the increased risk was about 60%.[4] However for type 1 diabetes, the prevalence is currently exhibiting insufficient evidence.[5] For *DM* patients with chronic foot ulceration, a study showed that this group had higher level of both depression and anxiety than in DM patients without complication.[6]

Generally for *DM* patient, previous studies showed prevalence of depression which varies from 11.5%,[7] 40.3%[8] and up to 47.9%.[6] While for *DM* patients with *DFU*, the prevalence rate of depression is much higher which ranges from 32.2%[9] up to 51.7%.[10] The prevalence of anxiety in *DM* population in a previous study showed that it varied from 30.5%,[7] 57.4%[11] up to 69.6%.[6]. While for anxiety in *DM* with *DFU*, a recent study showed its prevalence to be up to 36%.[12]

Sexual Dysfunction (*SD*) is a known diabetes-related complication that affects both male and female patients. *SD* can be potentially be associated in

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more people with DFU. For male with *DM*, it includes disorders of libido, ejaculatory problems, erectile dysfunction ("*ED*") and combination of the aforementioned conditions. The most common complaints reported was *ED*, about 35%-75% of patients with diabetes, compared to 26% in the general population.[13] Meanwhile, prevalence of female sexual dysfunction ("*FSD*") was 18.2% [14] and the common *SD* conditions reported were lack of sexual desire, sexual dissatisfaction, orgasmic disorder, pain, arousal disorder and poor lubrication.[13] There are few possible mechanisms resulting to these concerns; the first is through changes of blood supply to the urogenital tissue, which later will affect the genital lubrication. Secondly, DM also is known to cause neuropathic mediated alteration which affects the genital arousal response.[13, 14, 15] Depressive symptoms were positively associated with *ED*.[16,17] For *FSD*, psychological factors that associated were fear, depression, fatigue, stress, anxiety and belief.[18] Be that as it may, studies determining frequency of sexual dysfunction whether involving diabetic or nondiabetic women are largely limited.[15] Previous local study done in women with *DM* population showed that the prevalence of *FSD* was up to18.2%.[14]

In Malaysia, various studies have been carried out on the prevalence and risk factors of depression and anxiety among diabetics. However, the study on prevalence of depression and anxiety on diabetic patient with *DFU* is still lacking. In relation to sexual dysfunction, local data also limited especially for *ED* and *FSD* for *DM* patients in the presence of foot ulcer. This study therefore aims to compare the prevalence of anxiety and depression in *DM* patient with and without *DFU* as its primary objective. The secondary outcome is to know the prevalence of sexual dysfunction in both groups and at the same time to identify their associated factors for all outcomes. This study may help us to understand more about factors associated with depression, anxiety and sexual dysfunction in *DM* patients with and without foot ulcer.

MATERIALS AND METHODS

Ethical Consideration

Ethics committee of the Faculty of Medicine, University Kebangsaan Malaysia (FF-2015-212) and National Medical Research and Ethics Committee (MREC) of the Ministry of Health Malaysia (MOH), via the National Medical Research Registry (NMRR) has approved the study prior to its commencement (NMRR-15-1043-25205). Referral to the specialist centre was offered to participants who were detected to have psychiatric morbidity and sexual dysfunction.

Statistical Analysis

The data was analysed using the International Business Machine (IBM) Statistical Package for

Social Science (SPSS) version 23 (New York, USA). Numerical data was tested using Mann Whitney U analysis. Categorical variables of interest and their associated factors were calculated using chi-square test. Relationship between outcome variables analysed using simple logistic regression analysis and multiple logistic regressions were run to determine the predictor of associated factor. Two tails with alpha (α) values of 0.05 were used in all tests.

Study Design

A cross sectional study was carried out in outpatient clinic of medical and orthopedic departments in Hospital Raja Permaisuri Bainun (HRPB) Ipoh, Perak, once to twice per week from January 2016 to May 2016. A simple systematic randomization was done whereby every patient who went to the registration counter for normal clinic follow-ups with even number, regardless of clinic room was approached. For an example, the numbers 3022, 3024, 3026, etc., where the number '3' indicated clinic room number while the rest are the number of respective patients. The inclusion criteria were: (i) with DM; (ii) ages between 18-60 years old; (iii) fluent in local Malay language (able to read and understand the spoken language) and (iv) had given consent for this study. The exclusion criteria were: (i) refusal to give consent and (ii) not fluent in local Malay language.

Study Procedure

Those who have fulfilled the inclusion criteria were given questionnaires on socio demographic and HADS questionnaire to detect any psychiatric morbidity. Individual who was sexually active, ie. having sexual intercourse for at least once a month, was asked to complete IIEF 5 (male participants who were sexually active for the past 6 months) and MVFSFI (female participants who were sexually active for the past 4 weeks). The questionnaires involved in this study were all self-reporting, and a researcher was arranged to assist any participant who needs further clarification about the questionnaire. Those who had recent and previous history of DFU at the time of the study will be allocated to the DFU group, based on the questionnaire and additional confirmatory records by the said hospital.

Study Instrument

1. A self-constructed questionnaire on demographic and brief clinical detailed;
   The questionnaire was devised to obtain data such as gender, ethnicity, religion, marital status, education level, monthly household income, occupation and smoking status. The appropriate clinical data which were based on self-reporting included height (m), weight (kg),

duration of *DM* in years, other medical illness and *DFU* grading using Wagner's classification (Wagner WF, 1981).[19] For *DFU* grading, it was done by the doctor in charge of those who had ulcer problem. Records of the ulcer severity were traced in the patients' files or were inquired directly to the treating doctor.

2. Hospital Anxiety Depression Scale ("*HADS*");
   The Malay version of HADS is a valid screening tool for Malaysian population to identify depression and anxiety with sensitivity up to 90.0% and specificity of 86.2% for anxiety and sensitivity of 93.2% and specificity of 90.8% for depression with cutoff point 8/9.[20] The reason this scale was referred to in this study was because it carries a lower risk of confounding diabetes-related and psychological morbidity symptoms compared to some other widely used scales.[21] The scale has been validated for the Malaysian population in previous study.[22] It had good internal consistency reliabilities measured with Cronbach's alpha coefficient which were 0.86 and 0.78 for anxiety and depression respectively. The questionnaire had two sections – each with seven items for both Anxiety and Depression scale, which was rated using Likert scale; 0 (not at all) to 3 (almost always). The scores for anxiety and depression were categorized into three groups: (i) 0-7 "no risk", (ii) 8-10 "borderline risk" and (iii) ≥11 as "intermediate or severe risk" for both. Other ways to describe the anxiety and depression scores are using the following cut points: a score between 0 and 7 was classified as normal and a score between 8 – 21 points as increased risk. This had been used in this study for analysis.

3. International Index for Erectile Function (*IIEF 5*);
   IIEF-5 is an abbreviated version of the IIEF 15, which was the original instrument developed as a diagnostic tool for *ED* to complement clinical judgment. The IIEF-5 is a subset of IIEF 15 and it comprises items 2, 4, 5, 7, and 15, specifically for erectile function ("*EF*"). The Malay version of the IIEF-5 was acceptable measurement as the area under the ROC curve of the Malay IIEF-5 was 0.86; where the optimal cut-off score is 17, and the sensitivity and specificity was 85% and 75% respectively.[23] The items are rated on a 6 grade likert scale in which score ≤ 17 indicates presence of *ED*.

4. Malay version of Female Sexual Function Index (*MVFSFI*);
   MVFSFI is a 19-items questionnaire that is reliable and valid to be used among Malaysian community.[24] Sexual dysfunction will be present in those who score a total of 55 and lower with 99% sensitivity and 97% specificity. The following are the six domains of sexual function measured in MVFSFI and its cut-off score with sensitivity and specificity respectively: (i) desire; ≤5 for sexual desire disorder (sensitivity = 95%, specificity = 89%); (ii) arousal; ≤9 for sexual arousal disorder (sensitivity = 77%, specificity = 95%); (iii) lubrication; ≤10 for disorder of lubrication (sensitivity = 79%, specificity = 87%); (iv) orgasm; ≤4 for orgasmic disorder (sensitivity = 83%, specificity = 85%); (v) satisfaction; ≤11 for sexual dissatisfaction (sensitivity = 83%, specificity = 85%); and (vi) pain; ≤7 for sexual pain disorder (sensitivity = 86%, specificity = 95%).[24]

RESULTS

A total of 960 patients were encountered and 480 patients have been approached via simple randomization (refer to figure 1). About 50% of them did not fulfil the inclusion criteria as they either have no *DM*; as this study was conducted in general orthopedic clinic which may involve other limb problems not related to *DFU* and also in general medical clinic; which comprised of patients with various diagnosis including infectious diseases (i.e. hepatitis, AIDS etc.), thyroid disease, hematological disorder, rheumatologic disorder and etc., or that they were in extreme age group; i.e. older than 65 years of age or younger than 18 years of age as well as some who did not comprehend Bahasa Melayu. 31.7% of those approached were uninterested and had therefore declined their participation in the study. A total of 164 participants have fulfilled the inclusion criteria and were recruited in the study. However only 118 samples were able to give complete details of their weight and height (either based on participant own knowledge or tracing from the case note) whereas 62.8% (n=103) of the participant answered the questionnaire on sexual dysfunction which comprised of 74 respondents who completed the IIEF 5 and 29 respondent who completed the MVFSFI. Those who had not completed the questionnaires were not sexually active.
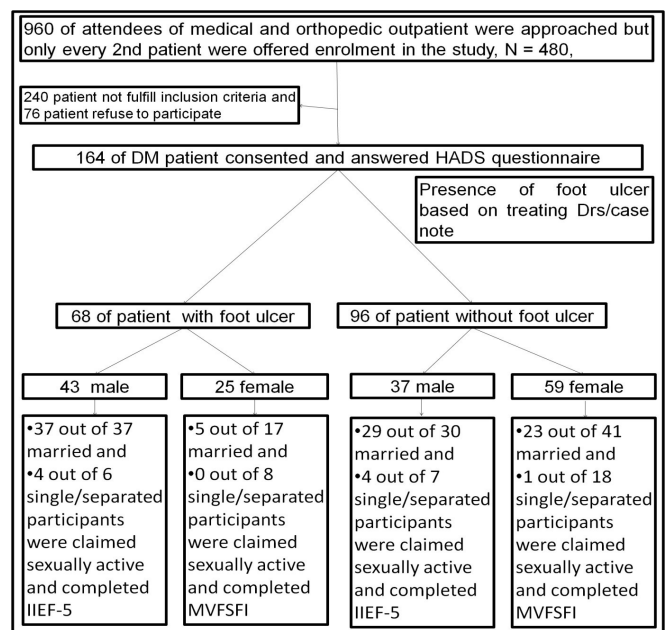

Figure 1 Flow chart of the study sample collections

Respondent characteristics

The median age of the *DM* participants was 56.0 years old (IQR=48-60.75) and comprised of 48.8% male and 51.2% female. Majority were Malay participants (56.1%), followed by Indian (27.4%), Chinese (14.6%) and others (1.8%). The same pattern is seen in the religious group, where Muslim (57.9%) are followed by Hinduism (22.6%), Buddhism (12.8%), Christianity (4.3%) and others (2.4%). Majority of the participants were married (76.2%) whereas 23.8% were either single or separated or divorced. 54.9% of participants' education level was limited up to secondary school and below, while 59.8% were unemployed. 75% of the participants earned less than RM3000 and 90.2% of them were currently not smoking. The median duration of *DM* for all samples was 10 years (IQR: 4-16) and about 63.4% of samples had other medical co-morbidity. The medical co-morbidity includes hypertension (HPT) 55.5%, Ischemic Heart Disease (IHD) 23.3% and others disease 29.9%. Among all *DM* participants, 41.5% had *DFU* and in contrast, 58.5% had no *DFU*. 31% of participants, who gave their weight and height had obese BMI. Among those who had *DFU*, more than 50% had grade 3 and higher BMI (Table 1).

Table I: Sociodemographic characteristic & prevalence risk of depression, anxiety & SD in DM patient with and without DFU

Presence DFU	Yes, N (%)	No, N (%)	P value	Crude OR	95% CI	Adjusted OR	95% CI	P value
Total of 164 DM participant	68(41.5)	96(58.5)						
Age Med (IQR)	56.0(51-63)	55.5 (47-60)	0.283* 0.169	1.024	0.990-1.060	-	-	-
Gender			0.002	2.743	1.444-5.211	6.317	1.975-20.205	0.002
Male	43(53.8)	37(46.3)						
Female	25(29.8)	59(70.2)						
Ethnicity			0.009	2.381	1.239-4.576	-	-	1.00
Malay	46(50)	46(50)						
Non Malay	21(29.6)	50(70.4)						
Religion			0.015	2.238	1.166-4.294	-	-	1.00
Muslim	47(49.5)	48(50.5)						
Non Muslim	21(30.4)	48(69.6)						
Marital status			0.420	1.358	0.646-2.858	-	-	-
married	54(43.2)	71(56.8)						
Single/divorced	14(35.9)	25(64.1)						
Educational level			0.077	2.028	0.926-4.441	6.014	1.360-26.585	0.018
Secondary school and lower	57(45.2)	69(54.8)						
Higher than secondary school	11(28.9)	27(71.1)						
Employment status			0.041	1.975	1.029-3.791	1.786	0.589-5.417	0.306
Employed	21(31.8)	45(68.2)						
Unemployed	47(48)	51(52)						
Household income			0.714	1.144	0.556-2.356	-	-	-
Less than RM3000	52(42.3)	71(57.7)						
More than RM3000	16(39)	25(61)						
Smoking status			0.212	1.939	0.685-5.493	-	-	-
Yes	9(56.3)	7(43.8)						
No	59(39.9)	89(60.1)						
BMI in kg/m² n=118	26.8(23.9-29.9)	28.2 (24.5-34.0)	0.154*	-	-	-	-	-
Obesity (BMI>30)			0.094	1.988	0.890-4.490	-	-	-
Yes	13(35.1)	24(64.9)						
No	42(51.9)	39(48.1)						
Medical Co morbid			0.344	1.370	0.714-2.630	-	-	-
Yes	46(44.2)	58(55.8)						
No	22(36.7)	38(63.3)						
Duration of DM in years	6.5(2.25-10.0)	10.0 (5.0-15.0)	0.787* 0.833	1.004	0.966-1.044	-	-	-
Duration of HPT in years	10.0(5.0-16.8)	10.0 (4.0-15.0)	0.019* 0.036	0.936	0.879-0.996	0.946	0.833-1.014	0.116
Duration of IHD in years	2.0(1.0-8.5)	5.0 (3.0-10.0)	0.041* 0.256	0.925	0.809-1.058	-	-	-
Others disease duration in years	5.0(1.5-13.0)	9.0 (4.3-11.5)	0.394* 0.844	0.993	0.926-1.065	-	-	-
DFU grading								
Grade 0	4 (5.9)							
Grade 1	11 (16.2)							
Grade 2	17 (25.0)							
Grade 3	15 (22.1)							
Grade 4	12 (17.6)							
Grade 5	9 (13.2)							

Con't

Depression				1.437	0.630-3.275	-	-	-
Yes	25(36.8)	36(37.5)	0.389					
No	43(63.2)	60(62.5)						
Anxiety				1.033	0.452-2.362	-	-	-
Yes	25(36.8)	37(38.5)	0.871					
No	43(63.2)	59(61.5)						
Sexual dysfunction (SD)			0.006¥	3.889	1.412-10.708	2.286	0642-8.145	0.202
n=103	40(52.6)	36(47.4)	0.009					
Yes	6(22.2)	21(77.8)						
No								
Female Sexual dysfunction (FSD) N=29	1(11.1)	8(88.9)	0.563	2.000	0.191-20.469	-	-	-
Yes	4(20.0)	16(80.0)						
No								
Domain								
Sexual Desire Disorder			0.661	1.750	0.143-21.384	-	-	-
Yes	2(16.7)	10(83.3)						
No	3(17.6)	14(82.4)						
Sexual Arousal Disorder			0.813	1.333	0.124-14.380	-	-	-
Yes	1 (14.3)	6(85.7)						
No	4(18.2)	18(81.8)						
Disorder of Lubrication			0.563	2.000	0.191-20.696	-	-	-
Yes	1 (14.3)	6(85.7)						
No	4(18.2)	18(81.8)						
Orgasmic Disorder			0.999	0.000	0.000	-	-	-
Yes	0(0)	6(100)						
No	5(21.7)	18(78.3)						
Sexual Pain Disorder			0.999	0.000	0.000	-	-	-
Yes	0(0)	8(100)						
No	5(23.8)	16(76.2)						
Sexual Dissatisfaction			0.563	2.000	0.191-20.969	-	-	-
Yes	1(11.1)	8(88.9)						
No	4(20)	16(80)						
Erectile dysfunction (ED) N=74			0.153	3.482	0.630-19.256	-	-	-
Yes	39(58.2)	28(41.8)						
No	2(28.6)	5(71.4)						

*Mann Whitney U Test
¥ Chi Square Test
DM = Diabetes-mellitus;
SD = Sexual Dysfunction
DFU = Diabetic Foot Ulcer
HPT = Hypertension

In the *DFU* group several patterns were noted which include more male than female participants (53.8% versus 29.8%, p=0.002, crude OR=2.74, 95% CI 1.44, 5.21), more Malay than non-Malay participants (50% versus 29.6%, p=0.009, crude OR=2.38, 95% CI 1.24, 4.58), similar pattern for Muslims than non-Muslims (49.5% versus 30.4%, p=0.015, crude OR=2.24, 95% CI 1.17, 4.29) and more were unemployed than employed (48% versus 31.8%, p=0.041, crude OR=1.98, 95% CI 1.03, 3.79). Other differences in *DFU* group such as severity in having more than one medical co-morbidity, BMI less than 30kg/m², smoking cigarette, married, having household income of less than RM3000 and education level of secondary school and lower, although these were found to be statistically insignificant.

There were significant differences for median duration of hypertension, HPT (10 years, IQR 5-12, p=0.02) and duration of ischemic Heart Disease, IHD (4.5 years, IQR 1.75-10, p=0.04) between participants with *DFU* than without *DFU*. Among all factors, only male gender (p value=0.013, OR=3.95, 95% CI 1.33, 11.70) and those with lower education status (AOR=6.0, p value = 0.018, 95%CI 1.36, 26.59) were significantly associated with *DFU*.

Prevalence and risk factors for depression and anxiety among DM respondents

Table 1 also showed prevalence of depression (36.8% and 37.5%, p value=0.92) and anxiety (36.8% and 38.5%, p value=0.82) of *DM* patients with and without *DFU* respectively. Both results were statistically insignificant. Overall prevalence of depression and anxiety among *DM* participants regardless of the presence of foot ulcer were 37.2% and 37.7% respectively (Table 2 and 3). While among participants who had *ED* and *FSD*, 38.8% and 44.4% respectively had depression and anxiety symptoms. For those with depression, 18.9% has borderline risk and 18.3% has intermediate to severe risk. For *DM* participants who had anxiety, 25% were borderline risk and 12.8% were intermediate to severe risk. Since the prevalence of depression and anxiety were insignificant between *DM* with and without *DFU*, thus the factors associated with depression and anxiety was carried out in all participants with *DM*.

Simple logistic regression analysis for *DM* patients with anxiety (refer table 3) showed significant determinant factors which comprises of (i) depression (p value<0.01, crude OR=7.01, 95%CI 3.46, 14.23), (ii) sexual pain disorder (p value=0.03, OR=7.08, 95%CI 1.17, 42.79) (iii) unemployment (p value=0.01, crude OR=2.66, 95%CI 1.38, 5.10) and (iv) cigarette-smoking participant (p value=0.04, OR=4.77, 95%CI 1.05, 21.77) were found significantly associated with anxiety.

Table II: Simple and multiple logistic analyses for factors associated with risk of depression in DM patient

Characteristic	Had Depression, N (%)	P value	Crude OR (95% CI)	Adjusted OR(95% CI)	P value
All DM participant (n=164)	61 (37.2)				
DFU		0.924	1.03(0.54-1.96)	-	-
Yes	25(36.8)				
No	36(37.5)				
Anxiety		<0.001	9.01(3.52-23.02)	30.91(2.06-462.83)	0.013
Yes	40(64.5)				
No	21(20.6)				
Sexual dysfunction (SD) N=101		0.025	3.75(1.18-11.93)	-	1.000
Yes	30(39.5)				
No	4(14.8)				
Female Sexual dysfunction (FSD) N=29		0.100	4.53(0.75-27.39)	-	-
Yes	4(44.4)				
No	3(15)				
Domain			-	-	-
Sexual Desire Disorder		0.331			
Yes	4(33.4)				
No	3(17.6)				
Sexual Arousal Disorder		0.030	8.44(1.23-58.16)	-	1.000
Yes	4(57.1)				
No	3(13.6)				
Disorder of Lubrication		0.442	2.00(0.34-11.70)	-	-
Yes	3(42.9)				
No	4(18.2)				
Orgasmic Disorder		0.558	1.80(0.25-12.85)	-	-
Yes	2(33.3)				
No	5(21.7)				
Sexual Pain Disorder		0.057	0.167(0.03-1.06)	-	-
Yes	4(50)				
No	3(14.3)				
Sexual Dissatisfaction		0.016	11.25(1.58-80.30)	7.680(0.11-555.68)	0.351
Yes	5(55.6)				
No	2(10)				
Erectile dysfunction (ED) N=74		0.228	0.26(0.03-2.31)	-	-
Yes	26 (38.8)				
No	1 (14.3)				
Gender		0.937	0.98(0.52-1.84)	-	-
Male	30(37.5)				
Female	31(36.9)				
Ethnicity		0.137	0.61(0.32-1.17)	-	-
Malay	39(42.4)				
Non Malay	22(31%)				
Religion		0.231	0.67(0.32-1.17)	-	-
Muslim	39(41.1)				
Non Muslim	22(31.9)				

Con't

Marital status		0.187	0.61(0.30-1.27)	-	-
Married	43(34.4)				
Single/divorced	18(46.2)				
Educational level		0.415	0.73(0.34-1.57)	-	-
Secondary school and lower	49(38.9)				
Higher than secondary school	12(31.6)				
Employment status		0.420	0.77(0.40-1.46)	-	-
Employed	27(40.9)				
Unemployed	34(34.7)				
Household income		0.227	1.60(0.75-3.43)	-	-
Less than RM3000	49(29.3)				
More than RM3000	12((39.8)				
Smoking status		0.569	0.74(0.26-2.10)	-	-
Yes	7(43.7)				
No	54(36.5)				
Obesity (BMI>30) N=118		0.716	0.86(0.39-1.91)	-	-
Yes	15(40.5)				
No	30(37)				
Medical Co morbid		0.438	0.77(0.40-1.50)	-	-
Yes	41(39.4)				
No	20(33.3)				

Table III: Simple and multiple logistic analyses for factors associated with risk of anxiety in DM patient

Characteristic	Had Anxiety	P value	Crude OR (95% CI)	Adjusted OR(95% CI)	P value
All DM participants	**62 (37.7)**				
DFU		0.817	1.08(0.57-2.05)	-	-
Yes	25(36.8)				
No	37(38.5)				
Depression		**<0.001**	**7.01(3.46-14.23)**	**8.67(3.96-18.97)**	**<0.001**
Yes	22(21.4)				
No	40(65.6)				
Sexual dysfunction (SD)		0.112	0.44(0.16-1.21)	-	-
Yes	30(39.5)				
No	6(22.2)				
Female Sexual dysfunction (FSD) N=29		0.301	0.42(0.08-2.20)	-	-
Yes	4(44.4)				
No	5(25)				
Domain		-	-	-	
Sexual Desire Disorder		0.999			
Yes	5(41.7)				
No	4(23.5)				
Sexual Arousal Disorder		0.100	0.22(0.04-1.33)	-	-
Yes	4(57.1)				
No	5(22.7)				
Disorder of Lubrication		0.858	0.86(0.16-4.62)	-	-
Yes	3(42.9)				
No	6(27.3)				
Orgasmic Disorder		0.270	0.35(0.06-2.25)	-	-
Yes	3(50)				
No	6(26.1)				
Sexual Pain Disorder		**0.033**	**7.08(1.17-42.79)**	2.45(0.47-12.81)	0.290
Yes	5(62.5)				
No	4(19)				
Sexual Dissatisfaction		0.065	0.20(0.04-1.11)	-	-
Yes	5(55.6)				
No	4(20)				

Erectile dysfunction		0.228	0.26(0.03-2.31)	-	-
Yes	26 (38.8)				
No	1 (14.3)				
Gender N=164		0.808	0.93(0.49-1.74)	-	-
Male	31(38.8)				
Female	31(36.9)				
Ethnicity		0.514	0.81(0.43-1.53)	-	-
Malay	37(40.2)				
Non Malay	25(35.2)				
Religion		0.723	0.89(0.46-1.53)	-	-
Muslim	37(38.9)				
Non muslim	25(36.2)				
Marital status		0.394	0.73(0.35-1.51)	-	-
Married	45(36)				
Single/divorced	17(43.6)				
Educational level		0.316	1.46(0.70-3.04)	-	-
Secondary school and	45(35.7)				
Higher than secondary	17(44.7)				
Employment status		**0.003**	**2.66(1.38-5.10)**	**3.20(1.49-6.91)**	**0.03**
Employed	34(51.5)				
Unemployed	28(28.6)				
Household income		0.195	0.62(0.30-1.28)	-	-
Less than RM3000	43(35)				
More than RM3000	19(46.3)				
Smoking status		**0.044**	**4.77(1.05-21.77)**	**8.51(1.59-45.56)**	**0.01**
Yes	2(12.5)				
No	60(40.5)				
Obesity (BMI>30) N=118		0.532	1.16(0.60-2.22)	-	-
Yes	15(40.5)				
No	28(34.6)				
Medical Co morbid		0.660	1.16(0.60-2.22)	-	-
Yes	38(36.5)				
No	24(40)				

However, multiple logistic regression analysis showed that (i) depressive symptom (p value<0.01, adjusted OR= 8.67, 95% CI 3.96-18.97), (ii) unemployment (p value=0.03, adjusted OR=3.20, 95% CI 1.49, 6.91) and (iii) smoking cigarette (p value=0.01, adjusted OR=8.51, 95% CI 1.59, 45.56) were significant determinant for anxiety in *DM* participant.

Meanwhile, anxiety (p value<0.01, crude OR=9.01, 95% CI 3.52, 23.02), sexual dysfunction (p value=0.03, crude OR=3.75, 95%CI 1.18, 11.93), sexual arousal disorder (p value=0.03, crude OR=8.44, 95% CI 1.23, 58.16) and sexual dissatisfaction disorder (p value=0.02, crude OR=11.25, 95% CI 1.58-80.30) were significantly associated in *DM* respondent with depression. From these factors, when further analysis was carried out via multiple logistic regression only anxiety (p value=0.01, adjusted OR=30.91, 95% CI 2.06, 462.83) was found to be a significant determinant factor for depression (refer table 2).

Prevalence & Risk of sexual dysfunction among respondent

Sexual dysfunction was more prevalent in *DFU* group (52.6% versus 47.4%, p value=0.01) whereas there is more *ED* in *DFU* group compared to non DFU group (58.2% versus 41.8%, p value=0.13) (refer to table 1). In male participants, 41 out of 43 (95.3%) in DFU group and 33 out of 37 (89.2%) in non DFU group responded to IIEF 5 questionnaire. Despite the finding not being statistically significant, it could be clinically significant as *ED* is a consequence of poor glycemic control and peripheral neuropathy in *DM* patient, [25] its prevalence will be more in *DFU* group as *DFU* is also a consequence of peripheral neuropathy[3], vasculopathy and poor glycemic control.[26]

In contrast,*FSD* was found to be more prevalent in non *DFU* group compared to DFU group (88.9% versus 11.1%, p value=0.56). Both findings were not statistically significant. The reason for this insignificant finding could be due to small sample size for *FSD* (n=29) as primarily the sample size calculated was based on prevalence of depression in *DM* with or without *DFU*, and had not considered the prevalence of sexual dysfunction in *DM* with or without *DFU*. Concluding *FSD* to be more prevalent in non *DFU* group is quite misleading as there are more who answered MVFSFI questionnaire in non *DFU* group, 24 out of 59 (40.7%) than in *DFU* group, 5 out of 25 (20.0%). The reason was many of them in *DFU* group are not sexually active especially female; hence they didn't answer the questionnaire. Therefore, the finding is only

significant when both male and female data were combined for *SD* and the results are only applicable for this study population rather than the general Malaysian population. In future, specific study can be done on sexual dysfunction with larger sample size.

For *DM* population, prevalence of *SD* was 73.8%, in which specifically for ED and FSD were 31% and 90.5% respectively (refer table 4). Among participants who had *ED* and *FSD*, 38.8% and 44.4%

respectively had depression and anxiety symptoms. Presence of *DFU* (p value=0.01, crude OR=3.89, 95% CI 1.41, 10.71), depressive symptoms (p value=0.02, crude OR=3.75, 95%CI 1.18, 11.93) and male gender (p value<0.01, crude OR=21.27, 95% CI 7.03, 64.33) were factors significantly associated with *SD*. From these factors, only depressive symptoms (p value=0.025, adjusted OR=4.42, 95%CI 1.08, 18.16) and male gender (p value=0.001, adjusted OR=18.42, 95%CI 5.51, 61.62) were more likely to have *SD*.

Table IV: Simple and multiple logistic analyses for factors associated with SD in DM patient

Factors	Had SD, N (%)	P value	Crude OR	95% CI	P value	AOR	95% CI	P value
DM participants N=103	76(73.8)							
DFU presence		0.006	3.89	1.41-10.71	0.009	1.87	0.53-6.68	0.333
Yes	40(87.0)							
No	36(63.2)							
Depression		0.019	3.75	1.18-11.93	0.025	4.42	1.08-18.16	0.039
Yes	30(88.2)							
No	46(66.7)							
Anxiety		0.106	2.283	0.83-6.31	0.112	-		-
Yes	30(83.3)							
No	46(68.7)							
Gender		<0.001	21.27	7.03-64.33	<0.001	18.42	5.51-61.62	<0.001
Male	67(90.5)							
Female	9(31)							
Ethnicity		0.809	0.895	0.37-2.19	0.809	-	-	-
Malay	14(24.6)							
Non Malay	12(26.7)							
Religion		0.432	0.702	0.29-1.70	0.433	-	-	-
Muslim	14(23.3)							
Non Muslim	13(30.2)							
Marital status		0.776	0.789	0.15-4.05	0.766	-	-	-
married	25(26.6)							
Single/divorced	2(22.2)							
Educational level		0.541	0.737	0.28-1.97	0.542	-	-	-
Secondary school and lower	19(24.7)							
Higher than secondary school	8 (30.8)							
Employment status		0.885	0.937	0.39-2.27	0.885	-	-	-
Employed	12(25.5)							
Unemployed	15(26.8)							
Household income		0.582	0.758	0.28-2.04	0.583	-	-	-
Less than RM3000	20(27.8)							
More than RM3000	7(22.6)							
Smoking status		0.275	0.427	0.09-2.04	0.287	-	-	-
Yes	2(14.3)							
No	25(28.1)							
Obesity (BMI>30)		0.213	1.93	-	-	-	-	-
Yes	14(60.9)							
No	42(75)							
Medical Co morbid		0.696	1.20	-	-	-	-	-
Yes	51 (75)							
No	25 (71.4)							

DISCUSSION

Diabetis is a chronic debilitating illness which can cause altered peripheral sensation of the foot, thus leading to actual ulceration process which may happen much earlier. Diabetic neuropathy and vasculopathy occurred when blood sugar is poorly controlled for prolonged periods of time.[3] Majority of those with *DFU* had *DM* for more than 10 years.[27] It is important to detect depression and anxiety in *DM* population as a whole as it affect compliance with the treatment regime leading to lower self-efficacy and to self-neglect, associated with higher morbidity, mortality and lower quality of life, even more in *DFU* group.[28, 29]

In this study it was shown that significant characteristic of *DFU* group were more male gender, Malay ethnicity, Muslim religion, unemployed and have lower educational status. Out of these features, only male and lower education status was more predictive for *DFU*. Findings was similar to one study done in Portugal, whereby in *DFU* group, males were two times more likely than female to be scheduled for amputation and more than half were retired and majority had lower education status.[30] However other study done by Mazlina et al locally and another study done in Egypt found no significant difference in terms of gender between patients with and without DFU.[27, 29] Other possible reason could be because there are more male participants, 43 out of 68 (63.2%) compared to female participants, 25 out of 68 (36.8%) in *DFU* group of this study.

In large epidemiological study done in Norway involving more than 60,000 participants with 3 arm designs, those without *DM*, *DM* without foot ulcer and *DM* with history of foot ulcer, found that levels of anxiety and depression and psychological well-being did not differ between the two diabetes groups.[31] Hence, the risk of depression and anxiety were similar regardless of the presence of *DFU*. Nevertheless, for *DM* population, the prevalence rate in this study was comparable to previous study done locally, which was 40.3% for depression, and 31.4% for anxiety.[8] Specifically for *DFU* group, prevalence of depression in this study was still comparable to a study done in London (32.2%)[9] and in Australia (51.7%).[10] While for anxiety in *DFU* group, prevalence in current study was also comparable to study done in Italy (36%).[12] Regarding to the unemployment rate, this was understandable as more DFU patients were not able to continue with their current work because of the impact of DFU itself. Futhermore, the median age of DFU group was 56 years old, and most of the samples were already retired and not working anymore. Study done by Mazlina M et al in 2011 also found that there were more unemployed participants in DFU although the difference was not statistically significant.[29]

Current study showed that there were no statistical difference between prevalence of depression and anxiety for DM patient with and without DFU. The primary interest of this study was to look for depression and anxiety risk in diabetes with foot ulcer and found it was similar to diabetes group without foot ulcer. The findings could give the impression that the presence of foot ulcer has nothing to do with depression and anxiety for DFU group and should not be generalized for Malaysian population. This is because the study was conducted only in one centre; therefore a multicentre study in future could be the better way to do the research.

For DM with risk of depression, anxiety was a significant determinant factor. This finding was similar with previous study done locally by Kaur et al 2013. Although the result was statistically significant, the broad CI gave negative impact on the result, i.e. the findings were less accurate. Therefore, the result needs to be interpreted carefully. On the other hand, those who had depressive symptom and unemployment were likely to have risk of anxiety in DM participant. Kaur et al 2013 found that unemployed DM patients were 1.2 to 1.6 times more likely to experience anxiety. Those who smoke cigarettes have more than 8 times higher risk to have anxiety in DM population, which is similar to previous study done in Ireland which found that smoking was a risk factor for higher anxiety in DM population.[28]

While for SD, its prevalence was found to be statistically significant in DFU group. DFU, FSD and ED were known complications of DM. This can be explained by the fact that DM may affect the neurovascular system (neuropathy and vasculopathy) of the respective organs. For FSD, the current study's finding was higher (31%) as compared to previous local study done in women with DM population 18.2%.[14] This is possible as prevalence of DM in Malaysia has been increasing year by year[1] and the current study combined groups of DM with and without DFU, while the previous study was done only in DM patient without DFU. Therefore, when looking at the prevalence of FSD in DM without DFU; it was 88.9% while for DM with DFU, its only 11.1% and the results were not significant.

Again the small sample size (n=29) who responded to the MVFSFI questionnaire may lead for thebiased result. However, the result is still comparable to previous study done in Italy which showed prevalence of FSD in DM women without complication as high as 75%.[32] Researchers also identified that the flaw of MVFSFI questionnaire was due to its design which was meant only for those who are sexually active; those who are not sexually active were not able to answer the questionnaire. Therefore it is difficult for the researcher to comment on this factor, as most who are not answering the MVFSFI questionnaire in DFU group are probably having the FSD more than non DFU group that could cause them to become non-sexually active.

On the other hand, for ED cases; previous study showed its prevalence in DM population range from 27% to 90%.[13, 33, 34, 35.] This study found higher prevalence of 90.5% of ED combining both DM patients with and without DFU, which is still comparable to previous findings. When looking at the separate groupings, prevalence of ED in DFU was only 58.2%, which is higher compared to 41.8% in group without DFU. This was expected as DFU is a complication of peripheral neuropathy, as previous study showed those with peripheral neuropathy, the odds of having ED was 5.22 (95%CI 1.14-21.89)[34] to 5.9 (95% CI 1.6-21.3).[36] Therefore, the current study adds on the prevalence of ED specifically for DFU population locally which was not done previously.

A study in Egypt found that psychological factors associated with FSD include fear, depression, fatigue, stress, anxiety and belief.[18] A study by Kalmbach DA et al 2012 found that in cases involving healthy young adults showed that most sexual problems among women was more uniquely related to anhedonic depression; while for men, there are more mixed relationship of anxiety and depression.[37] This study found that depressive symptoms and male gender were more likely to have SD in DM population. The result was affected by the main fact that participants who completed the questionnaire on SD were male who answered the IIEF 5 questionnaire.

In intimate relationships, both depression and anxiety are important psychological factors as causes and consequences of relationship distress. Previous local study found depressive symptoms to be positively associated with ED in aging population[16, 17] and not for DM population, while a systematic review on risk factors for ED in Type 2 DM found that age, duration of illness, presence of peripheral neuropathy and BMI had positive association with erectile dysfunction.[25]

This study has several limitations. Firstly, the patients were recruited through a single centre i.e. the outpatient clinic of Medical and Orthopaedic departments of Hospital Raja Permaisuri Bainun Ipoh, Perak and hence the results cannot be generalized to other Malaysian population and also due to the modest sample size of patients. Secondly, this study did not distinguish between different types of diabetics, and most of the results involved Type 2 diabetics.

CONCLUSION

This study identified that the prevalence of depression and anxiety for diabetic patients, both with and without foot ulcer was similar. Male and lower education status was significantly associated with DFU. While depression, unemployment and smoking cigarette became significant risk factors for anxiety in DM, anxiety became significant risk factor for depression in DM. There was a significantly high prevalence of sexual dysfunction in DM with foot ulcer as both were the result of diabetes complication. For sexual dysfunction in DM, depression and male gender were significant risk factors. Overall, by identifying the prevalence and the risk factors involved, early detection and treatment for depression and anxiety may improve health outcomes, including sexual functions. However further studies are required to ascertain the directional nature of this relationship.

Conflict of Interest
Nil

Abbreviation and symbols
Body Mass Index, BMI
Confidence Interval (CI)
Diabetic foot ulcer (DFU)
Diabetes Mellitus (DM)
Erectile Function (EF)
Erectile Dysfunction (ED)
Female Sexual Dysfunction (FSD)
Hospital Anxiety and Depression Scale (HADS)
Hospital Raja Permaisuri Bainun (HRPB)
Hypertension (HPT)
International Index for Erectile Function 5 (IIEF-5)
International Business Machine (IBM)
Interquartile Range (IQR)
Ischemic Heart Disease, IHD
Median (Med)
Medical Research and Ethics Committee (MREC)
Ministry of Health Malaysia (MOH)
National Medical Research Registry (NMRR)
Odd Ratio (OR)
Sexual Dysfunction (SD)
Statistical Package for Social Science (SPSS)

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