RESEARCH ARTICLE

PREVALENCE OF MAJOR DEPRESSIVE DISORDER AND ITS ASSOCIATION WITH ERECTILE DYSFUNCTION AMONG CLIENTS ON METHADONE MAINTENANCE THERAPY

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Abstract

Major Depressive Disorder (MDD) is substantially higher in people seeking Methadone Maintenance Therapy (MMT) as compared to the normal population. Erectile Dysfunction (ED) is one of the side effects of Methadone Maintenance Therapy (MMT) which is rarely explored as it is regarded as a sensitive topic. This study aims to determine the prevalence of MDD and its association with ED among MMT clients. A cross-sectional study was conducted involving 160 subjects who attended the Methadone outpatient clinic. The clients were given Patient Health Questionnaire-9 to screen for depressive symptoms and MINI International Neuropsychiatric Interview to diagnose MDD. ED was diagnosed using the 5-item International Index of Erectile Function. The results showed the prevalence of depression in clients on MMT was 30.6% and the prevalence of ED was 72.5%. On multivariate analyses, there were significant associations between ED with depression (P<0.05). Smoking also was found to be contributed to depression. Sociodemographic factors, comorbid medical illnesses, and illicit substance use were found to have no associations with depression. Therefore, given the prevalence of MDD and ED in MMT clients was high, routine assessment of depressive symptoms and sexual function in clients on methadone should be done to minimize their negative impact on the clients. ***ASEAN Journal of Psychiatry, Vol. 22(4), June 2021: 1-17.***

Keywords: Depression, Erectile Dysfunction, Methadone, Opioid User, Sexual Dysfunction, Smoking

Introduction

Globally, the use of opiates had affected 16.5 million people, or 0.4% of the population aged between 15 to 64 years old. High prevalence of its use reported in the regions of South-West and Central Asia, Eastern and South-Eastern Europe as well as North America [1]. In Malaysia, the cumulative number of registered substance abusers between 1988 to 2006 was 300,241 and 60.7% of them were opioid users. In the number had increased to 75% [2]. Methadone Maintenance Therapy (MMT) program was introduced in 2005 as part of the National Harm Reduction Program in Malaysia in response to rising numbers of opioid users [3]. Methadone has several adverse effects which include nausea, vomiting, constipation, drowsiness, abdominal pain, QTc prolongation, and sexual dysfunction [4].

Among the commonest side effect of sexual dysfunction is erectile dysfunction. A systemic review and meta-analysis involving 17 studies demonstrated that testosterone level was suppressed in men with chronic and regular opioid use which leads to ED [5]. Earlier studies have reported that higher methadone dosage (80-150 mg/day) was associated with lower plasma testosterone [6]. Studies had been more consistent in reporting no correlation between the duration of methadone treatment and ED [7,8].

Testosterone deficiency symptoms are fatigue, weakness, mood disturbances, and sexual problems such as a decrease in libido and erectile dysfunction [9]. The chronic stimulation of the μ-opioid receptors by methadone also alters the function of the tuberoinfundibular axis and the dopaminergic control of prolactin, with a consequential impact on sexual functioning [10]. Among methadone clients, the worldwide prevalence of ED ranged from 52.8% to 75.7% [11]**.** In Malaysia, the prevalence of ED in methadone clients was between 67% to 68.5% [12,13]. However, only 3% reported that they had been asked about their sexual relationships by the addiction services [14] and sexual problems were often unexplored and the neglect was more pronounced in Asian populations due to it being regarded as a sensitive subject [15,16].

Major Depressive Disorder (MDD) was the most common mental illness in Malaysia affecting approximately 2.3 million people and the prevalence was estimated to be around 8% and 12% [17]. Globally, the prevalence of MDD ranges between 32.9% to 63.3% among methadone clients [18,19]. In the local setting, MDD was the most prevalent psychiatric disorder in clients on MMT ranging from 10.2% to 44.4% [18,19]. The development of MDD in drug abusers resulted from a familial and social problems as well as biological changes due to prolonged drug use. Studies showed there was significantly smaller grey matter volume (GMV) in multiple cortices, especially in the left inferior frontal gyrus and left cerebellar vermis in the MMT group compared to healthy subjects [20-22]. The smaller GMV in the pre-frontal cortices, left subcallosal, left insula, left post-central gyrus, cingulate gyrus, and right cerebellar declive correlated with higher depression scores. Thus there were significant structural differences in the emotion circuit and cerebellum between heroin-dependent patients on MMT and healthy controls [23,24]

Hallinan et al found that men on MMT had a high prevalence of ED, related to hypogonadism and depression compared to clients on Buprenorphine Maintenance Treatment. In a cross-national study conducted in Brazil, Italy, Japan, and Malaysia, depression was shown to be associated with erectile dysfunction and those with erectile dysfunction were 2.09 times more likely to have depression [25]. Similarly, Shiri et al., found a strong association between depressive symptoms and ED and this relationship was also bidirectional [26]. Also found a strong relationship between psychological distress and ED [27]. However, local studies showed contradicting results whereby it found no association between ED and depression among MMT clients. Hence, to resolve the disparity, this study aimed to determine the prevalence of MDD and its association with ED among MMT clients.

Methods

This was a cross-sectional observational study using a simple random sampling method conducted in Hospital Tengku Ampuan Rahimah (HTAR)**.** Methadone Maintenance Therapy Outpatient clinic in HTAR has been established for about 15 years, led by an addiction psychiatrist, medical officers, nurses, and medical attendants with total registered male clients of 236. The participants of the study were recruited within the period between 1st Jun 2020 to 31st August 2020. The inclusion criteria were clients who were 18 years old and above having a sexual partner (defined as a person engaged in sexual activity with the client) and able to give informed consent and understand Malay or English language. Clients who were experiencing withdrawal, intoxication, active

psychosis, irritable or agitated were excluded. Clients with an existing diagnosis of erectile dysfunction were excluded. Clients having chronic and severe medical illnesses such as chronic cardiovascular disease, cerebrovascular disease, respiratory disease, renal disease, urinary tract disease, autoimmune disease, and malignancy were excluded. Ethics approval was obtained from the Ministry of Health Medical Research and Ethics Committee (KKM/NIHSEC/P20-89(8) and Universiti Teknologi MARA Research Ethics Committee (REC/03/2020 FB/46).

The clients attending Methadone outpatient clinic who fulfilled the selection criteria and consented to participate in the study were given the Patient Health Questionnaire-9 (PHQ-9) and the International Index of Erectile Function-5 (IIEF-5) scale meanwhile the socio-demographic and clinical factors questionnaires were filled up by the researcher. The Patient Health Questionnaire-9 (PHQ-9 is a self-administered questionnaire used to screen the presence and the severity of depression [28]. The Malay version of PHQ-9 developed by Sherina et al was used [29]. Those who scored four and above for depressive symptoms were interviewed using MINI Neuropsychiatry Interview (MINI) 6.0 to confirm the diagnosis of MDD.

The MINI is a short, structured diagnostic interview tool for psychiatric disorders in Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) and International Classification of Diseases-Tenth Edition (ICD 10) which was developed by Sheehan and colleagues in 1998 [30,31]. The translated MINI Malay version is acceptable and clinically relevant in making a diagnosis of major depressive disorder [32]. The International Index of Erectile Function-5 (IIEF-5) was given to assess for erectile dysfunction. It was developed by Raymond C. Rosen in 1996. The erectile function was explored using an abridged five-item version of the International Index of Erectile Function (IIEF-5), a self-administered questionnaire that explores the quality of erectile function and sexual intercourse confidence and satisfaction for the past six months [33]. The validated in Malay version developed by was used.

The data were analyzed using the Statistical Package for Social Sciences (SPSS) version 25.0 (IBM). Variables were described as mean ± standard deviation (±SD) for continuous data and number (n) and percentage for dichotomous or nominal data. The factors associated with MDD were analyzed using simple logistic regression (SLogR) followed by the hierarchical method of multiple logistic regression (MLogR). The socio-demographic factors, clinical factors, and presence of ED being the independent variables were entered into the SLogR. Variables with a p-value of less than 0.25 from the SLogR were subsequently included in the MLogR analysis. Model fitness was checked using the Hosmer-Lemeshow goodness of fit test. Confounders were adjusted; interactions, multicollinearity, and assumptions were also checked. The p-value of less than 0.05 with a confidence interval of 95% was taken as statistically significant.

Results

Prevalence of MDD and ED

74 participants had mild to severe depressive symptoms on the PHQ-9 and among them 30.6% (n=49) (95% CI: 23.5–37.7) were diagnosed to have major depressive disorder. The prevalence of ED in this study was 72.5% (n=116) (95% CI: 65.6–79.4). There were 40 % of the participants (95% CI: 27–52.0) who had a mild degree of erectile dysfunction and 22.5 % (95% CI: 16.0–30.0) of them had mild to moderate level of erectile dysfunction. While 8.1% (95% CI: 2.0–14.0) of them had moderate erectile dysfunction and 1.9% (95% CI: 2.3–3.5%) had severe erectile dysfunction.

Sociodemographic and Clinical Characteristic

A total of 160 participants were involved in this study with the age ranging from 25 to 76 years old. The sociodemographic characteristics and clinical features are shown

in Table 1. About two-thirds of the participants were more than 40 years old with a mean age of 44.81 ± 10.2 years. More than two-thirds of the participants were Malay (70%) and 71.2% were employed. 65% of the participants received a secondary education and 3% received tertiary education. Employment profiling revealed that 114 (71.2%) were employed and 46 (28.8%) were unemployed.

Table 1. Background characteristics of the patients (N=160)

Variables	n (%)	Range	Mean (SD)
Sociodemographic characteristics			
Age		25-76	44.81 (10.02)
≤ 30 years old	11 (6.9)		
31 – 40 years old	47 (29.4)		
41 – 50 years old	61 (38.1)		
≥51	41 (25.6)		
Ethnicity			
Malay	112 (70.0)		
Chinese	32 (20.0)		
Indian	14 (8.8)		
Others	2 (1.2)		
Education level			
None	4 (2.5)		
Primary	48 (30)		
Secondary	104 (65.0)		
Tertiary	4 (2.5)		
Employment Status			
Employed	114 (71.2)		
Unemployed	46 (28.8)		
Marital status			
Single	67 (41.9)		
Married	68 (42.5)		
Widow	10 (6.3)		
Separated	5 (3.1)		
Divorced	10 (6.2)		
Income (RM)		0-RM 5000	1010.38 (977.73)
0-1000	85 (53.1)		
1001-2000	61 (38.1)		
More than 2000	14 (8.8)		
Clinical factors			
Methadone duration (year)		0.1-15	4.83 (3.71)
Current Methadone dose (mg)		2 -130	54.22 (26.93)
Smoking			

Non-smoker	27 (16.9)		
Smoker	133 (83.1)		
Heroin			
No	130 (81.2)		
Yes	30 (18.8)		
Cannabis			
No	159 (99.4)		
Yes	1 (0.6)		
Stimulants			
No	144 (90.0)		
Yes	16 (10.0)		
Cocaine			
No	160 (100.0)		
Yes	0		
Benzodiazepines			
No	155 (96.9)		
Yes	5 (3.1)		
Alcohol			
No	141 (88.1)		
Yes	19 (11.9)		
Diabetes Mellitus			
No	154 (96.2)		
Yes	6 (3.8)		
Hypertension			
No	137 (85.6)		
Yes	23 (14.4)		
Dyslipidemia			
No	156 (97.5)		
Yes	4 (2.5)		
Hepatitis B			
No	151 (94.4)		
Yes	9 (5.6)		
Hepatitis C			
No	124 (77.5)		
Yes	36 (22.5)		
HIV			
No	141 (88.1)		
Yes	19 (11.9)		

The duration of methadone use was between one month to 15 years and the mean duration of usage was 4.83 (±3.71) years. The methadone dose prescribed was between 2 to 130 mg and the mean methadone dose is 54.22 (±26.93) mg.

More than three-quarters of the clients were smokers (133; 83.1%) and 44.4% of clients were concomitantly using other illicit substances. 42.2% of clients took heroin, followed by alcohol (27%), stimulant (22.5%),

benzodiazepine (7%), and cannabis (1%). There were 40% (64 clients) of the clients have existing comorbid medical illnesses with the highest recorded comorbidity was hepatitis C (56.2%) followed by hypertension (36%), HIV (29.6%), hepatitis B (9%), Diabetes mellitus (6%) and dyslipidaemia (4%).

Factors Associated With MDD in MMT Clients

The results of bivariate analysis between sociodemographic factors with MDD. In the socio-demographic characteristics, there were three significant factors have been found. These were age (OR: 2.2 (95% CI: 1.03-4.63), p: 0.04), employment status (OR: 0.26 (95%CI: 0.12-0.53), p <0.001) and income (OR: 0.37 (95% CI: 0.18-0.76), p: 0.006). The other factors were not statistically significant (Table 2).

Table 2. Association between sociodemographic characteristics and major depressive disorder (N=160)

Characteristics		Depression				
		Non depressed	Depressed	X^2	OR	*p*-value
	n	(N=101),	(N=49),	(df)	(95%CI)	
		n (%)	n (%)			
Age				4.227	2.182	0.040*
40 and less	58	46 (79.3)	12 (20.7)	-1	(1.028, 4.632)	
More than 40	102	65 (63.7)	37 (36.3)			
Ethnicity						
Malay	112	79 (70.5)	33 (29.5)	0.237	0.835	0.627
Non-Malay	48	32 (66.7)	16 (33.3)	-1	(0.405, 1.724)	
Education level				1.886	0.613	0.17
Primary and less	53	33 (62.3)	20 (37.7)	-1	(0.305, 1.236)	
Secondary and more	107	78 (72.9)	29 (27.1)			
Employment				14.111	0.257	<0.001*
Employed	114	89 (78.1)	25 (21.9)	-1	(0.124, 0.534)	
unemployed	46	22 (47.8)	24 (52.2)			
Marital status				2.802	0.55	0.094
Married	68	52 (76.5)	16 (23.5)	-1	(0.272, 1.112)	
Single/ Divorced/ Widow/widower	92	59 (64.1)	33 (35.9)			
Income (RM)				7.501	0.375	0.006*
1000 and less	85	51 (60.0)	34 (40.0)	-1	(0.184, 0.765)	
More than 1000	75	60 (80.0)	15 (20.0)			

Note: [f] *p*-value based on fisher's exact test; *: $p<0.05$; OR=odd ratio; CI: confidence interval

The results of bivariate analysis between clinical factors with MDD. There were seven significant factors have been found. There were: smoking status (OR: 0.4 95% (CI: 0.17-0.93), p: 0.03), stimulant usage (OR: 3.34 (95% CI: 1.17-9.58), p: 0.019), heroin usage (OR: 3.36 (95% CI: 1.48-7.61), p: 0.003), benzodiazepines usage (OR: 9.78 (95%CI: 1.06, 89.90), p=0.03),

Hepatitis C status (OR: 2.2 (95% CI: 1.02-4.75), p=0.041), HIV status (OR: 8.48 (95%CI: 2.85-25.23), p:<0.001) and ED (OR: 14.30 (95% CI: 2.3.30, 61.97), p:<0.001) (Table 3).

Table 3: Association between clinical factors and major depressive disorder (N=160)

Characteristics		Depression				
				X^2	OR (95%CI)	*p*-value
	n	Non depressed	Depressed	(df)		
		(N=101), n (%)	(N=49), n (%)			
Methadone duration (years)				0.741	1.371 (0.668, 2.816)	0.389
				-1		
< 5	112	80 (71.4)	32 (28.6)			
> 5	48	31 (64.6)	17 (35.4)			
Current methadone dose				2.92	2.076 (0.888, 4.849)	0.088
				-1		
< 80 mg	133	96 (72.2)	37 (27.8)			
> 80 mg	27	15 (55.6)	12 (44.4)			
Smoking				4.694	0.400 (0.171, 0.932)	0.030*
				-1		
Non-smoker	27	14 (51.9)	13 (48.1)			
Smoker	133	97 (72.9)	36 (27.1)			
Heroin				8.962	3.359 (1.481, 7.618)	0.003*
				-1		
No	130	97 (74.6)	33 (25.4)			
Yes	30	14 (46.7)	16 (53.3)			
Stimulants				5.494	3.343 (1.166, 9.580)	0.019*[f]
				-1		
No	144	104 (72.2)	40 (27.8)			
Yes	16	7 (43.8)	9(56.2)			
Benzodiazepines				5.922(1)	9.778 (1.063, 89.900)	0.031*
No	155	110 (71.0)	45 (29.0)			
Yes	5	1 (20.0)	4 (80.0)			
Alcohol				0.009(1)	1.052 (0.375, 2.951)	0.923
No	141	98 (69.5)	43 (30.5)			
Yes	19	13 (68.4)	6 (31.6)			
Diabetes Mellitus				3.811(1)	4.844 (0.857, 27.395)	0.051
No	154	109 (70.8)	45 (29.2)			
Yes	6	2 (33.3)	4 (66.7)			
Hypertension				0.219(1)	1.249 (0.491, 3.174)	0.64
No	137	96 (70.1)	41 (29.9)			
Yes	23	15 (65.2)	8 (34.8)			
Dyslipidemia				0.725(1)	2.319 (0.317, 16.959)	0.395[f]

No	156	109 (69.9)	47 (30.1)			
Yes	4	2 (50.0)	2 (50.0)			
Hepatitis B				0.857(1)	1.884 (0.484, 7.344)	0.458[f]
No	151	106 (70.2)	45 (29.8)			
Yes	9	5 (55.6)	4 (44.4)			
Hepatitis C					2.206 (1.023, 4.758)	0.041*
No	124	91 (73.4)	33 (26.6)	4.175(1)		
Yes	36	20 (55.6)	16 (44.4)			
HIV				18.815(1)	8.480 (2.850, 25.229)	<0.001*
No	141	106 (75.2)	35 (24.8)			
Yes	19	5 (26.3)	14 (73.7)			
Erectile Dysfunction				19.428 (1)		
Yes	116	69(59.5)	47(40.5)		14.304(3.302,61.974)	<0.001*
No	44	42(95.5)	2(4.5)			

Note. [f]: *p*-value based on fisher's exact test; *: $p<0.05$; OR: odd ratio; CI: confidence interval

The bivariate analysis had identified variables as potential covariates for the multivariate analysis at an alpha level of 0.25. In multiple logistic regression analysis, adding the erectile dysfunction to the first model explained 19.9% (Nagelkerke R^2) of variance in major depressive disorder. In this model, erectile dysfunction was noted to be a factor contributing to MDD. Adding the sociodemographic characteristics to the second model explained 29.6% (Nagelkerke R^2) of variance in major depressive disorder. In this model, the significant predictors were identified to be erectile dysfunction and employment status. In the third model, adding the substance usages explained 41.2% (Nagelkerke R^2) of variance in major depressive disorder. In this model, the significant predictors were identified to be erectile dysfunction, smoking, and heroin usage. While adding the medical comorbidities in the fourth model (final model) explained 43.7% (Nagelkerke R^2) of variance in the major depressive disorder. The final model indicated that smoking and erectile dysfunction are the factors contributing to major depressive disorder in this study. The summary of the final model is shown in (Table 4).

Table 4. Summary of variables predicting for major depressive disorder (n=160)

Variables	**B**	**S.E.**	**Wald**	**Adjusted OR**	***p*-value**	**95% CI**	
						Lower	**Upper**
ED status	-2.412	0.813	8.808	0.09	0.003*	0.018 - 0.441	
[yes]							
Diabetes Mellitus	-1.303	1.05	1.54	0.272	0.215	0.035 - 2.127	
[no]							
Hepatitis C	-0.075	0.557	0.018	0.928	0.893	0.312 - 2.763	
[no]							
HIV	-1.179	0.75	2.47	0.307	0.116	0.071 - 1.338	
[no]							
Age	-0.303	0.505	0.361	0.739	0.548	0.275 - 1.985	

[40 and less]						
Education	-0.563	0.52	1.171	0.569	0.279	0.205 - 1.579
[primary and none]						
Employment status	0.73	0.573	1.626	2.076	0.202	0.675 - 6.381
[unemployed]						
Marital status	0.022	0.486	0.002	1.022	0.964	0.394 - 2.650
[single/widow/ separated/ divorcee]						
Income (RM)	0.313	0.558	0.314	1.367	0.575	0.458 - 4.083
[1000 and less]						
Methadone dose	-0.748	0.623	1.44	0.473	0.23	0.140 - 1.606
[80 mg and less]						
Smoking	1.165	0.574	4.121	3.206	0.042*	1.041 - 9.872
[non-smoker]						
Heroin	-0.967	0.587	2.712	0.38	0.1	0.120 - 1.202
[no]						
Stimulants	-1.251	0.701	3.182	0.286	0.074	0.072 - 1.132
[no]						
Benzodiazepines	-1.416	1.309	1.17	0.243	0.279	0.019 - 3.159
[no]						

Note: 1.*: $p<0.05$ 2. [reference category] 3. Dependent variable: Major depressive disorder 4. Independent variables: erectile dysfunction, age, education, employment status, marital status, income, methadone dose, smoking, heroin, stimulants, benzodiazepines, diabetes mellitus, hepatitis C, HIV.

Discussion

In our study, 30.6% of the participants were diagnosed to have major depressive disorder. The result was comparable to a study by Baharuddin et al, where it reported a prevalence of 32.6% for MDD among methadone clients assessed by Structured Clinical Interview for DSM-IV (SCID-I). The diagnosis of MDD in this study was made using the same population setting, in an outpatient methadone clinic in Klang Valley. Furthermore, the abovementioned population has a similar sociodemographic profile, as a majority of them were male, Malay, and received secondary education. On the other hand, Brienza et al found 42% of methadone clients were depressed. The findings were slightly higher than our research prevalence of MDD possibly due to differences in population in the United States, with the predominantly white race, and the study also included almost half of female clients. The rate of depression was known to be higher in the US and among females which may directly contribute to their findings [34]. In our study, the prevalence of ED among methadone clients was 72.5% (mild ED, 40%; mild to moderate ED, 22.5%; moderate ED, 8.1%; severe ED, 1.9%). The result was comparable with a previous local study done in which the rate of ED among men on MMT was 68.5% (mild ED, 36.1%; mild to moderate ED, 22.2%; severe ED, 3.7%). The prevalence was also in concordance with a study by Teoh et al that revealed the prevalence of ED of 67%.

After controlling for other variables in the final regression model, apart from ED, smoking was shown to contribute to depression Smokers on MMT have an increased odds of 3.2 times to develop depression in our study. The prevalence of smokers in our study was 83% which

corresponds to a local study which found 81% prevalence of tobacco use disorder in MMT clients [35]. There were limited studies on smoking contribution to depression among methadone patient, however, in the general population, the lifetime prevalence of MDD was high in cigarette smoker. The estimated MDD prevalence ranged between 31% and 60% in chronic smokers who smoked at least 1 pack per day [36]. It was estimated that smokers have an almost twofold greater risk of becoming depressed than non-smokers [37]. In a systematic review, reported evidence in support of a bidirectional relationship between depression and smoking in which nearly half of the studies reported that baseline depression was associated with later smoking behaviour, whether it would be the onset of smoking itself, increased smoking heaviness, or the transition into dependence. Smoking exposure at baseline was also associated with later depression, supporting the alternative hypothesis that prolonged smoking increases susceptibility to depression. It also supported a self-medication model, suggesting that individuals smoked to ease psychiatric symptoms [38]. Nicotine was found to have both acute and chronic mood-elevating properties resulted from nicotinic receptor activation that augments the release of dopamine, norepinephrine, and serotonin neurotransmitters at the cellular level which contributed to its' antidepressant properties [39].

Erectile dysfunction was shown to be associated with MDD in our study. Our findings were in concordance with previous studies. A study in India, which had reported sexual dysfunction assessed using the International Index of Erectile Function-15 (IIEF-15) and Arizona Sexual Experiences Scale revealed sexual dysfunctions were 3.2 times more prevalent in the depressed population as compared to the control group among methadone clients [40]. Another study in China found a strong relationship between psychological distress and ED, therefore emphasizing the importance of both diagnosis and management of ED among methadone patients receiving long-term MMT. The depression in MMT clients may be a consequence of erectile dysfunction, or depression may cause erectile dysfunction in which it showed bidirectional causal relation. Testosterone deficiency symptoms also directly caused fatigue and mood disturbances including depression. It is common for men with ED to feel angry, frustrated, in which such feelings may lead to a lack of self-esteem and was shown to have an impact on intimate relationship, impaired the quality of life (QOL), and eventually leads to depression in methadone clients [41]. In the MMT population, only 18.5% of clients sought medical treatment as ED was regarded as not a serious condition and due to their hesitancy [42]. Eventually, harbouring and repression of the sexual frustration may contribute further to depression in methadone clients.

Comorbid medical illnesses, such as HIV, hepatitis, hypertension, and DM and concomitant substance use were not significantly contributed to depression. Our findings were similar to previous studies that found medical history and concomitant substance use shows no association with depression. In the general population, however, chronic medical illnesses such as diabetes, hypertension, or infectious disease such as HIV and hepatitis highly associated with depression. In the current study, there were possibilities that chronic medical illnesses were underreported by the participants. The data on medical co-morbidities were obtained by subjects' self-report, which might not reflect the true number of respondents with medical illnesses. As the majority of the participants were more than 40 years of age, they might already have a chronic disease that was not screened or diagnosed. In our study population, the prevalence of hypertension, diabetes mellitus, and dyslipidaemia were 14.4%, 3.8%, and 2.5% respectively. Further biological investigation in MMT clients could identify those with medical co-morbidities accurately. The prevalence of Hepatitis C, HIV, and Hepatitis B were 22.5%, 11.8%, and 5.6% respectively in our study. The findings were in concordance to study by Rao et al and postulated that lower percentage of infectious disease was likely due to the positive outcome of harm reduction program that significantly reduced the number of intravenous drug use [43].

The strength of our study includes diagnostic assessment of MDD rather than screening for

depressive symptoms [44,45]. We also use translated and validated instruments in Malay language and a random sampling method in recruiting participants. There were important significant associations found which are modifiable and treatable [46,47]. These findings highlight the need for further research on the interaction between smoking, erectile dysfunction, and mental health, with implications for prevention, diagnosis, and treatment. So far, this study is among the first local study to found the association between smoking and ED with depression in MMT clients.

A few limitations were noted in this study including a small sample size. This study was performed at a single center in an urban area and it is a cross-sectional study, thus narrowing the generalizability of the study findings and might not demonstrate the cause-and-effect relationship respectively between ED and depression [48-51]. Another limitation was the use of a self-report questionnaire for assessing erectile dysfunction which leads to a potential for response bias, as respondents may inaccurately report their symptoms. Chronic medical illness (DM, HPT, Dyslipidemia) should be assessed and validated as the reported prevalence was low. Finally, multiple confounding factors were not studied such as family history, psychosocial issue, other comorbid psychiatry illness, and amount and chronicity of cigarette smoking that contribute to depression. Further exploration of other correlates for erectile dysfunction in the MMT clients in the context of a biopsychosocial approach should be considered as well.

Conclusion

In conclusion, methadone clients in treatment should be routinely screened for both depression and erectile dysfunction, given its high prevalence in this population. Detecting both disorders is essential for initiating treatment as it will affect the prognosis and treatment outcome.

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