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ORIGINAL RESEARCH

The Association Between Medication Adherence, Internalized Stigma and Social Support Among Outpatients with Major Depressive Disorder in a Malaysian Hospital: A Cross-Sectional Study

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Background: Internalized stigma and medication non-adherence pose significant challenges for treating major depressive disorder (MDD), leading to disability, increased suicide risk, and morbidity. Limited data exists on modifiable factors associated with adherence in lower-resourced settings like Malaysia. This study aimed to investigate poor adherence prevalence and the demographic and clinical factors associated with poor medication adherence among patients with MDD.

Methods: This cross-sectional survey recruited participants using universal sampling from a major hospital in Selangor, Malaysia. Participants answered questionnaires consisting of demographic and clinical information (medical history, duration of anti-depressant treatment for MDD, psychiatric ward admission history, and any medication side effects experienced), the Internalized Stigma of Mental Illness Scale (comprising alienation, stereotype, perceived discrimination, and social withdrawal), the Multidimensional Scale of Perceived Social Support (comprising family, friend, and significant other support), and the Malaysia Medication Adherence Assessment Tool. Simple and multiple logistic regression and mediation analyses were conducted.

Results: Of the 268 participants (69% female), 57.1% were suboptimally or moderately adherent to their medication. Buddhists (adjusted odds ratio [a*OR*] = 0.280, 95% *CI* [0.115, 0.679], $p = 0.005$), higher family support (a*OR* = 0.753, 95% *CI* [0.591, 0.960], $p = 0.022$), a history of ward admissions (a*OR* = 3.523, 95% *CI* [1.537, 8.072], $p = 0.003$), and higher internalized stigma (a*OR* = 2.828, 95% *CI* [1.497, 5.344], $p = 0.001$) were significantly associated with low/moderate medication adherence. The effect of internalized stigma subdomains (alienation, perceived discrimination, and social withdrawal) on medication adherence were partially mediated by family support.

Conclusion: More than half of the participants demonstrated low to moderate medication adherence. Those with higher internalized stigma demonstrated higher odds of low/moderate medication adherence, but this effect was attenuated by family support. Therefore, internalized stigma and family support are important points of consideration when assessing patients with MDD in Malaysia.

Keywords: medication adherence, MDD, internalized stigma, social support, Malaysia

Introduction

Depression, a widespread mental disorder with worldwide implications, affected approximately 280 million people globally in 2019.[1] The aftermath of the 2020 COVID-19 pandemic has intensified the prevalence of depression, resulting

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in a 25% increase in the global occurrence of depression and anxiety.[2] Depression is also associated with higher mortality risk, as depressive disorders are associated with suicide and other causes of mortality.[3,4]

Antidepressant medication is a common and evidence-based approach to treating individuals with MDD, including in Lower- and Middle-Income Countries (LMICs) such as Malaysia.[5] Among the critical issues related to depression treatment, patients' poor adherence to antidepressant medications plays a crucial role in many cases of nonresponse, acute relapses, recurrences in the long term, and increased morbidity, comorbidity, and mortality.[6] Many studies showed that functional recovery takes longer than syndromic remission, mainly due to residual depressive symptoms and quality-of-life deficits affecting depressed patients for extended periods,[7] highlighting the need for adequate and persistent antidepressant treatment.

Medication Nonadherence in Patients with MDD

Medication adherence refers to the ability of a patient to comply with medication instructions and persistence in continuing the medication until otherwise instructed.[8] In LMICs, the prevalence of medication nonadherence is higher than in high-income countries.[9,10] This may have occurred due to low knowledge and negative attitudes and beliefs about medication in LMICs.[11] A study in Malaysian older adults found that only 50.6% of the participants recorded high medication adherence.[12]

Studies have demonstrated that non-adherence with MDD medications is common, including in Malaysia.[13] A systematic review found that as many as 50% of patients with major depressive disorder were medically nonadherent.[13] In Malaysia, there is a marked lack of study on medication adherence in patients with MDD. In a study by Teeng et al among patients with depression, although the primary focus of the study was on the intervention's effectiveness, the baseline medication adherence data (60.2% in the intervention group and 37.1% in the control group) reflected the adherence difference between the two groups prior to the intervention.[14]

Medication nonadherence is multifactorial, which includes patient-related factors (misperceptions about the medication, side effects, and lack of tolerability), clinician-related (eg, insufficient instruction given, lack of decision-making and follow-up care), and structural factors (eg, access, cost, social support, and stigma).[15] Several pre-existing factors are associated with medication nonadherence, such as gender and age.[16] A study by Ho et al[17] found that Malaysian who were of Malay and Chinese ethnicity had a larger proportion of being non-adherent to antidepressants than Indians. The authors also found that medication side effects were a major barrier to medication adherence.[17]

Internalized Stigma and Medication Adherence

Understanding the modifiable factors such as stigma could be beneficial as points of assessment and intervention. Stigma has been shown to be a barrier against medication adherence.[18–20] Stigma refers to experiences involving shame, dishonor, or disapproval that may lead to someone to be rejected, subjected to discrimination, and cut off from society.[21,22] Stigma is associated with lower knowledge about mental health.[23] Self-stigma, also known as internalized stigma, refers to the cognitive and affective process through which individuals with mental illness assimilate and adopt the negative societal views directed against them.[24]

Several studies have found an association between internalized stigma and medication nonadherence. A study in China on people living with major depressive disorder found that higher internalized stigma, but not perceived stigma, was significantly associated with lower medication adherence.[19] Similarly, a Southwestern Ethiopian study among individuals with mental illness revealed that higher self-stigma was associated with higher non-adherence.[18] Another study on patients with tuberculosis showed that depression was associated with lower medication adherence in those with higher stigma.[20] This association may be accounted for by the fact that stigma is a barrier to seeking medical help and gives rise to misconceptions about the mental disorder, thus leading to defaulted treatment or non-adherence.[25]

In Malaysia, several qualitative studies have explored the reasons underlying medication nonadherence in patients with depression. A study by Ho et al revealed that stigma about taking antidepressants decreased their adherence; it was inconvenient taking their medication in front of friends due to the need of keeping their illness a secret.[17] In another qualitative study among Malaysians with chronic depression, stigma against mental illness may lead to a wish to stop taking antidepressants as soon as possible, which is a potential cause for nonadherence.[26] These studies reveal a need to

further confirm quantitatively the association between internalized stigma and medication nonadherence among patients with MDD in Malaysia.

Social Support and Medication Adherence

Social support is another modifiable factor associated with medication adherence; higher social support is associated with higher medication adherence.[13,27] As medication adherence requires both compliance and persistence to a medication regimen,[8] social support which provides emotional encouragement, practical assistance, and informational aid could assist a patient with depression to understand and be on track of their medication regimen.[28,29] However, studies on antidepressant medication adherence, in particular, found mixed results in their association with social support. A study among US older adults found that in people with low social support, African American women had lower odds of antidepressant medication nonadherence compared to white males and females.[28] On the other hand, a study in Korea found no significant association between perceived social support and antidepressant medication.[30]

Social support has also been studied as a mediator in medication adherence among patients with depression. A study in the US by Tovar et al among patients with comorbid depression and diabetes found that social support from family and friends fully mediated the relationship between depression and diabetes care adherence.[31] However, there is a lack of studies which explored the mediating role of social support in the relationship between internalized stigma and antidepressant medication adherence. The mixed results reported above also warrant further investigation into the relationship between social support and antidepressant medication adherence in Malaysia.

Considering the limited data on potentially modifiable factors that drive poor adherence in Malaysia, we conducted a cross-sectional survey of poor adherence prevalence and of demographic, clinical factors including standardized assessments of medication adherence, internalized stigma and social support among a Malaysian outpatient sample with MDD. In addition, the mechanism behind which internalized stigma is associated with medication adherence is not well explored, especially in examining the role of different types of social support. Social support and internalized stigma are important considerations for medication adherence in this country, as Malaysia practices a collectivistic culture; individuals with a mental disorder may be more likely to have internalized stigma in such a culture, but social support may be particularly important to mitigate the effect of internalized stigma on adherence in this context.[26,32] We hypothesized that social support (from family significant others, and friends) will significantly mediate the effect of internalized stigma subscales (alienation, stereotype, perceived discrimination, social withdrawal, and stigma resilience) on medication adherence.

Materials and Methods

Study Design and Site

This was a cross-sectional study conducted at the outpatient department of the psychiatry clinic in Hospital Kajang. Hospital Kajang is a government hospital under the Ministry of Health Malaysia. It is one of the teaching hospitals located in the east part of Kajang Town, in the Hulu Langat district, Selangor.

Study Population

This study employed universal sampling of all adult outpatients with a diagnosis of MDD who fulfilled the inclusion and exclusion criteria during the three-month study period (April to June 2023). Inclusion criteria were (1) follow-up patients at the outpatient clinical who fulfilled the criteria of major depressive disorder based on the Diagnostic and Statistical Manual of Mental Disorders, Version 5, Text-Revision (DSM-5-TR);[33] (2) 18 years old and above; (3) were prescribed anti-depressant medication; and (4) can read either English or Malay language. Those who declined to participate in the study, were non-literate, could not understand English or Malay language, had underlying organic brain disease, were acutely psychotic, or had intellectual disability were excluded.

Sample Size

The sample size needed for this study was calculated using a sample size calculator.[34] Based on the assumption of 95% confidence interval, 5% margin of error, and the expected prevalence of 22.1% for individuals with internalized stigma,[35] a minimum of 268 participants were needed for this study.

Study Instruments

All study instruments were self-administered in the English or Malay languages, based on the participants' preference.

Participant Sociodemographic and Clinical Characteristics

Sociodemographic characteristics of the participants that were collected were sex, age group (18–25, 26–30, or > 30 years old), race (Malay, Chinese, Indian, or others), religion (Islam, Buddhism, Hinduism, Christianity, or others), employment status (employed, unemployed, pensioner, or student), marital status (single, married, or others), education level (primary, secondary, or tertiary), income (Bottom 40%, Middle 40%, or Top 20%), and living arrangement (living alone, with family or with friends). Clinical variables such as medical history (with or without comorbid diseases), family history of mental illness (yes or no), duration of anti-depressant treatment for MDD (< 5 years, 5 to 10 years, 10 to 20 years, or > 20 years), psychiatric ward admission history (yes or no), and any medication side effects experienced during their medication treatment (yes or no) were also obtained from the survey questionnaire.

Malaysia Medication Adherence Assessment Tool (MyMAAT)

MyMAAT is a self-administered questionnaire developed by Hatah et al[36] that consists of 12 items to measure medication adherence, available bilingually in English and Malay. This questionnaire was developed in Malaysia. Each question is a 5-point Likert item from 5 (”strongly disagree”) to 1 (”strongly agree”). The total score was the sum of the marks for the individual items ranging between 12 and 60. Medication adherence was categorized as good adherence (total score ≥ 54) and moderate/poor adherence (total score < 54). The higher the score, the higher the medical adherence. The scale has excellent internal consistency with Cronbach's alpha coefficient of 0.91 and stable reliability. The sensitivity was 82.7% and the specificity of 49.2% when tested against the pharmacist's subjective assessment.[36]

The Internalized Stigma of Mental Illness Scale (ISMI)

ISMI developed by Boyd et al,[37] which measures internalized stigma of mental illness, consists of 29 items self-rated on a Likert scale of 1 (“Strongly disagree”) to 4 (“Strongly agree”) that assess five domains of internalized stigma. The alienation subscale is a measure of the subjective experience of being less than a full member of society. The stereotype endorsement subscale measures the degree to which the respondent agrees with common stereotypes about people with mental illness. The perceived discrimination experience subscale measures the respondent's perception of current treatment by others. The social withdrawal subscale measures avoidance of social situations because of mental illness. The stigma resistance subscale is a reverse-scored measure of the experience of not being affected by internalized stigma. Except for the stigma resistance domain, a higher score of the remaining four subscales indicates higher internalized stigma. The total score of each subscale is divided by the number of answered items. A higher score indicates a higher internalized stigma in a domain; a cut-off score of 2.51 and above was used to indicate high internalized stigma.[38] For this study, we used English and Malay versions of the scale. The English version has good internal reliability and validity.[37] The Malay version of ISMI is validated and showed excellent internal consistency (Cronbach's alpha = 0.91) and concurrent validity.[39]

Multidimensional Scale of Perceived Social Support (MSPSS)

MSPSS developed by Zimet et al[40] is used to assess perceived social support among the participants. It consists of 12 items, a self-administered measure of perceived adequate support from family, friends, and significant others using 7 points from 1 (“Very strongly disagree”) to 7 (“Very strongly agree”). The total MSPSS score ranged from 12 to 84 points; a score of 12–35 indicates low perceived support, 36 to 60 medium perceived support, and 61 to 84 high perceived support. The higher score indicates a greater perceived adequacy of social support from each of the three sources. It has a good internal reliability coefficient of 0.85. The Malay version of MSPSS showed good to excellent

internal consistency (Cronbach alpha of 0.93 for significant others, 0.88 for family and 0.96 for friends, and test-retest reliability of 0.77.[41]

Data Collection

The study identified and recruited participants who fulfilled the inclusion and exclusion criteria. The patients who fulfilled the diagnosis of MDD based on DSM-5 criteria were identified from the archival notes and approached. Participants then were provided with the information and an explanation about the study and consent was obtained from the patient who agreed to participate. Participation was voluntary and participants could withdraw from the study anytime without any penalties. Participants who consented were then required to answer a set of pre-constructed questionnaires using a paper form.

Data Analysis

Data analysis was executed with IBM SPSS version 28.[42] For continuous data, skewness and kurtosis of <±2 and <±7 respectively were used to determine data normality.[43] Descriptive statistics were used to examine demographic and clinical characteristic data. For descriptive analysis, mean and standard deviation were used for continuous data, and frequencies were used for categorical data. Chi^2 test of independence was used to measure the associations between categorical variables, while independent samples *t*-test were employed to examine if internalized stigma and perceived social support were significantly different between moderate/low adherence and good adherence groups. Equality of variances was assumed if the Levene statistic was non-significant. If significant, Welch's *t*-test was performed instead of independent *t*-test. Simple and multiple logistic regression analyses were used to examine factors that were associated with moderate/low medication adherence. Finally, continuous scores will be used to estimate the mediation effect of family, significant other and friend social support on the relationship between internalized stigma subscales (alienation, stereotype, perceived discrimination, social withdrawal, and stigma resilience) and medication adherence. The level of significance, the *p*-value was set at < 0.05, two-tailed.

SmartPLS, version 4.1.0.9[44] was used to perform the mediation analysis with 10,000 bootstrapped samples, using percentile bootstrap at one-tailed. PLS-SEM was adopted as it allows the indirect effect to be tested across multiple predictors in a single model, therefore reducing Type I measurement error. The measurement model was assessed from four aspects, ie, the item loadings, construct reliability, convergent validity, and discriminant validity. The item loadings should be at least 0.708 to show that the construct explains more than half of the indicator's variance.[45] The construct should also achieve a value between 0.70 and 0.95 for good composite reliability.[45] An average variance extracted (AVE) value of more than 0.50 is acceptable to indicate the presence of convergent validity. The heterotrait-monotrait ratio (HTMT) of correlations was used to determine discriminant validity, which requires a value lower than 0.90.[45] The structural model was then assessed after evaluating the measurement model. Common method bias and multicollinearity issues are absent if the value for the inner variance inflation factor (VIF) is less than 3.3.[46]

Results

A total of 270 participants were recruited in the study from the outpatient psychiatric clinic of Hospital Kajang. Two participants opted out of the study citing that they found answering the ISMI questionnaire distressing. These participants were debriefed and provided with a referral for follow-up if they found the need. Of the remaining 268 participants, most were female (69%), aged more than 30 years old (50.0%) and Malay/Muslim (70.5%). With regards to marital status, more than half (50.7%) were married, 57.8% were employed, 51.9% were from the middle- and higher-income categories, and 63.1% lived with their family. About one-third had secondary education, while 41.8% were degree holders. With regards to the participants' clinical characteristics, a majority reported no comorbidities (73.1%), no psychiatric ward admission in the past (81.7%), and most reported no side effects from antidepressant medication (63.8%). More than one-third was in antidepressant treatment for less than five years (39.2%), and 6.7% reported having received treatment for more than 20 years (Table 1).

More than half of the participants were suboptimally or moderately adherent to their medication (57.1%). Chi^2 test of independence showed that in terms of race, more Malays and Indians had moderate/low adherence, compared to the

Table 1 Socio-Demographic and Clinical Characteristics of the Participants and Associations with Medication Adherence (*N* = 268)

Variable	Total (%)	Medication Adherence		Chi^2 (*df*)	*p*
		Good (%)	Moderate / Low (%)		
Sex				0.137 (1)	0.712
Male	83 (31.0)	37 (44.6)	46 (55.4)		
Female	185 (69.0)	78 (42.2)	107 (57.8)		
Age group				5.639 (2)	0.060
19–25 years old	78 (29.1)	29 (37.2)	49 (62.8)		
26–30 years old	56 (20.9)	19 (33.9)	37 (66.1)		
> 30 years old	134 (50.0)	67 (50.0)	67 (50.0)		
Race				9.149 (2)	0.010
Malay	189 (70.5)	73 (38.6)	116 (61.4)		
Chinese	50 (18.7)	31 (62.0)	19 (38.0)		
Indian	29 (10.8)	11 (37.9)	18 (62.1)		
Religion				9.314 (3)	0.025
Islam	189 (70.5)	73 (38.6)	116 (61.4)		
Buddha	38 (14.2)	24 (63.2)	14 (36.8)		
Hindu	27 (10.1)	10 (37.0)	17 (63.0)		
Christian	14 (5.2)	8 (57.1)	6 (42.9)		
Marital status				3.148 (2)	0.207
Married	136 (50.7%)	58 (42.6)	78 (57.4)		
Single	128 (47.8%)	57 (44.5)	71 (55.5)		
Divorced/widowed	4 (1.5%)	0 (0.0)	4 (100.0)		
Occupation				3.646 (2)	0.162
Employed	155 (57.8)	70 (45.2)	85 (54.8)		
Unemployed/Pensioner	83 (42.2)	37 (44.6)	46 (55.4)		
Student	30 (11.2)	8 (26.7)	22 (73.3)		
Living arrangement				1.730 (2)	0.421
Living alone	36 (13.4)	19 (52.8)	17 (47.2)		
Living with friends	63 (23.5)	27 (42.9)	36 (57.1)		
Living with family	169 (63.1)	69 (40.8)	100 (59.2)		
Education level				4.365 (4)	0.359
Primary	11 (4.1)	3 (27.3)	8 (72.7)		
Secondary	86 (32.1)	39 (45.3)	47 (54.7)		
Certificate	14 (5.2)	4 (28.6)	10 (71.4)		
Diploma	45 (16.8)	16 (35.6)	29 (64.4)		
Degree	112 (41.8)	53 (47.3)	59 (52.7)		
Income				5.339 (1)	0.021
Bottom 40%	129 (48.1)	46 (35.7)	83 (64.3)		
Middle 40% and Top 20%	139 (51.9)	69 (49.6)	70 (50.4)		
Comorbidity				0.095 (1)	0.758
Yes	72 (26.9)	32 (44.4)	40 (55.6)		
No	196 (73.1)	83 (42.3)	113 (57.7)		
Family history of mental illness				0.774 (1)	0.379
Yes	106 (39.6)	42 (39.6)	64 (60.4)		
No	162 (60.4)	73 (45.1)	89 (54.9)		
Treatment duration (years)				3.171 (3)	0.366
< 5 years	105 (39.2)	50 (47.6)	55 (52.4)		
5 to 10 years	94 (35.1)	34 (36.2)	60 (63.8)		
10 to 20 years	51 ()19.0	24 (47.1)	27 (52.9)		
> 20 years	18 (6.7)	7 (38.9)	11 (61.1)		

(*Continued*)

Table 1 (Continued).

Variable	Total (%)	Medication Adherence		Chi^2 (*df*)	*p*
		Good (%)	Moderate / Low (%)		
History of ward admission				12.394 (1)	< 0.001
Yes	49 (18.3)	10 (20.4)	39 (79.6)		
No	219 (81.7)	105 (47.9)	114 (52.1)		
Medication side effects				3.833 (1)	0.050
Yes	97 (36.2)	34 (35.1)	63 (64.9)		
No	171 (63.8)	81 (47.4)	90 (52.6)		

Chinese, where there is a larger proportion of those who had good adherence (Chi^2 (2) = 9.149, $p = 0.010$). In terms of religion, Buddhists and Christians had a larger proportion of participants who had good adherence, while the opposite was true for Malay and Hindu participants (Chi^2 (3) = 9.314, $p = 0.025$). With regards to income, a larger proportion of those within the B40 income group recorded moderate/low adherence compared to those from other income groups (Chi^2 (3) 9.314, $p = 0.021$). Finally, those with a history of ward admission had a higher proportion of participants who had moderate/low adherence compared to those who did not have a history of ward admission (Chi^2 (1) 12.394, $p < 0.001$) (Table 1).

Data exploration showed that all continuous variables in this study were normally distributed, with skewness and kurtosis within the <±2 and <±7 ranges, respectively. The results of the independent samples or Welch's *t*-test showed that the full-scale score of internalized stigma (t (261.44) = −6.439, $p < 0.001$), and its subscales of alienation (t (266) = −6.321, $p < 0.001$), stereotype (t (266) = −5.092, $p < 0.001$), perceived discrimination (t (265.99) = −4.477, $p < 0.001$), social withdrawal (t (266) = −5.872, $p < 0.001$), and stigma resistance (t (266) = −4.569, $p < 0.001$) mean scores were significantly higher in the moderate/low adherence group than those in the good adherence group. In terms of social support, the results showed that the full-scale score of perceived social support (t (266) = 3.793, $p < 0.001$), family support (t (266) = 4.723, $p < 0.001$), and other sources of support (t (266) = 2.998, $p = 0.003$) had significantly lower mean scores in the moderate/low medication adherence group compared to the good adherence group (Table 2).

The results of the simple logistic regression showed that age group, race, religion, income group, history of ward admission, internalized stigma (and its subscales), and social support and its subscales (family and other support) were significantly associated with moderate/low medication adherence. Based on these significant results, a multiple regression

Table 2 Level of Internalized Stigma, Social Support and Associations with Medication Adherence (*N* = 268)

Variable	Mean (*SD*)	Medication Adherence		t Statistic (*df*)	*p*
		Good Mean (*SD*)	Moderate / Low Mean (*SD*)		
Internalized stigma	2.28 (0.533)	2.06 (0.454)	2.44 (0.529)	−6.439 (261.44)	< 0.001
Alienation	2.508 (0.783)	2.18 (0.708)	2.75 (0.748)	−6.321 (266)	< 0.001
Stereotype	2.01 (0.533)	1.83 (0.461)	2.15 (0.543)	−5.092 (266)	< 0.001
Perceived discrimination	2.03 (0.599)	1.85 (0.485)	2.16 (0.642)	−4.477 (265.99)	< 0.001
Social withdrawal	2.49 (0.752)	2.19 (0.699)	2.71 (0.717)	−5.872 (266)	< 0.001
Stigma resilience	2.46 (0.445)	2.33 (0.430)	2.57 (0.429)	−4.569 (266)	< 0.001
Social support	47.51 (13.526)	51.03 (12.632)	44.86 (13.608)	3.793 (266)	< 0.001
Family	4.08 (1.365)	4.52 (1.294)	3.75 (1.328)	4.723 (266)	< 0.001
Friend	3.58 (1.499)	3.72 (1.563)	3.48 (1.444)	1.345 (266)	0.180
Significant others	4.22 (1.485)	4.53 (1.473)	3.99 (1.455)	2.998 (266)	0.003

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model was fitted to identify factors significantly associated with moderate/low medication adherence. The model was significant (Chi^2 (10) = 65.92, $p < 0.001$), and the significant results of the Hosmer and Lemeshow tests indicated a good model fit. The exposure variables explained 29.5% of the variation in medication adherence (Nagelkerke's $R^2 = 0.293$). Internalized stigma and its subscales were entered separately into the model due to high intercorrelations of > 0.70. Buddhists (a*OR* = 0.280, 95% *CI* [0.115, 0.679], $p = 0.005$) recorded lower odds of moderate/low medication adherence. On the other hand, those with a history of ward admissions had the highest odds of moderate/low medication adherence (a*OR* = 3.523, 95% *CI* [1.537, 8.072], $p = 0.003$), followed by higher internalized stigma (a*OR* = 2.828, 95% *CI* [1.497, 5.344], $p = 0.001$).

With regards to the subscales of internalized stigma, all the subscales within internalized stigma were significantly associated with medication adherence in the multiple logistic regression analysis, except stigma resilience. Stereotypes demonstrated the highest odds among internalized stigma subscales (a*OR* = 2.240, 95% *CI* [1.221, 4.110], $p = 0.009$), followed by alienation (a*OR* = 1.997, 95% *CI* [1.330, 2.998], $p = 0.001$), social withdrawal (a*OR* = 1.871, 95% *CI* [1.223, 2.863], $p = 0.004$), and discrimination (a*OR* = 1.742, 95% *CI* [1.015, 2.991], $p = 0.044$) (Table 3).

Within the perceived social support variable, only family social support remained significant in the fully adjusted model, where higher family support was associated with lower odds of low/moderate medication adherence (a*OR* = 0.753, 95% *CI* [0.591, 0.960], $p = 0.022$). Support from significant others had become non-significant (Table 3).

Table 3 Level of Internalized Stigma, Social Support and Associations with Moderate/Low Medication Adherence (N=268)

Variable	Crude *OR*	95% *CI*		*p*	a*OR*	95% *CI*		*p*
		Lower	Upper			Lower	Upper	
Sex								
Male (ref)	1.000							
Female	1.103	0.655	1.860	0.712				
Age group								
19–25 years old	1.690	0.955	2.989	0.072	1.151	0.576	2.301	0.690
26–30 years old	1.947	1.018	3.725	0.044	1.882	0.896	3.954	0.095
> 30 years old (ref)	1.000				1.000			
Race								
Malay (ref)	1.000							
Chinese	0.386	0.203	0.733	0.004				
Indian	1.030	0.460	2.304	0.943				
Religion								
Islam (ref)	1.000				1.000			
Buddha	0.367	0.178	0.755	0.006	0.280	0.115	0.679	0.005
Hindu	1.070	0.465	2.464	0.874	0.843	0.320	2.219	0.729
Christian	0.472	0.157	1.415	0.180	0.617	0.180	2.120	0.443
Marital status								
Married (ref)	1.000							
Single/divorced/widowed	0.978	0.603	1.587	0.930				
Occupation								
Employed (ref)	1.000							
Unemployed/Pensioner	1.024	0.599	1.750	0.931				
Student	2.265	0.950	5.399	0.065				
Living arrangement								
Living alone	0.617	0.300	1.272	0.191				
Living with friends	0.920	0.512	1.653	0.780				
Living with family (ref)	1.000							

(*Continued*)

Table 3 (Continued).

Variable	Crude *OR*	95% *CI*		*p*	aOR	95% *CI*		*p*
		Lower	Upper			Lower	Upper	
Education level								
Primary (ref)	1.000							
Secondary	0.452	0.112	1.820	0.264				
Certificate/Diploma/Degree	0.503	0.129	1.964	0.323				
Income								
Bottom 40%	1.779	1.089	2.904	0.021	1.273	0.701	2.311	0.427
Middle 40%/	1.000							
Top 20% (ref)								
Comorbidity								
Yes	0.918	0.533	1.582	0.758				
No	1.000							
Family history of mental illness								
Yes	1.250	0.760	2.055	0.379				
No	1.000							
Treatment duration (years)								
< 5 years	1.000							
5 to 10 years	1.604	0.908	2.834	0.103				
10 to 20 years	1.023	0.523	1.999	0.948				
> 20 years	1.429	0.514	3.970	0.494				
History of psychiatric ward admission								
Yes	3.592	1.708	7.556	0.001	3.523	1.537	8.072	0.003
No	1.000				1.000			
Medication side effects								
Yes	1.668	0.998	2.788	0.051				
No	1.000							
Internalized stigma	4.769	2.754	8.260	< 0.001	2.828	1.497	5.344	0.001
Alienation	2.862	1.980	4.136	< 0.001	1.997	1.330	2.998	0.001
Stereotype	3.626	2.109	6.235	< 0.001	2.240	1.221	4.110	0.009
Discrimination	2.610	1.638	4.160	< 0.001	1.742	1.015	2.991	0.044
Social withdrawal	2.695	1.871	3.883	< 0.001	1.871	1.223	2.863	0.004
Stigma resistance	3.722	2.041	6.788	< 0.001	2.005	0.986	4.080	0.055
Social support	0.965	0.946	0.984	< 0.001	0.978	0.943	1.016	0.251
Family	0.645	0.531	0.783	< 0.001	0.753	0.591	0.960	0.022
Friend	0.895	0.760	1.053	0.179				
Others	0.777	0.656	0.920	0.003	0.923	0.742	1.148	0.470
Constant					0.459			0.505

Notes: Chi^2 (10) = 65.92, $p < 0.001$; Nagelkerke's $R^2 = 0.293$.
Abbreviations: a*OR*, adjusted odds ratio; *CI*, confidence intervals.

Mediation analysis using Partial Least Squares Structural Equation Modeling (PLS-SEM) was conducted to examine the indirect effect of family support in the relationship between internalized stigma subscales (alienation, stereotype, perceived discrimination, and social withdrawal) and medication adherence. Stigma resilience, friend support, and significant other support were excluded from further analysis due to non-significant relationships with medication adherence in the regression analyses.

The measurement model was evaluated before exploring the structural relationships between the latent variables. For the stereotype domain in the internalized stigma scale, five out of seven items have outer loadings of less than the cut-off criteria (0.708), with the lowest at 0.391. The AVE for stereotype was also less than 0.50 (AVE = 0.460); therefore, this domain was excluded from the mediation model. Although the outer loadings for one item from perceived discrimination

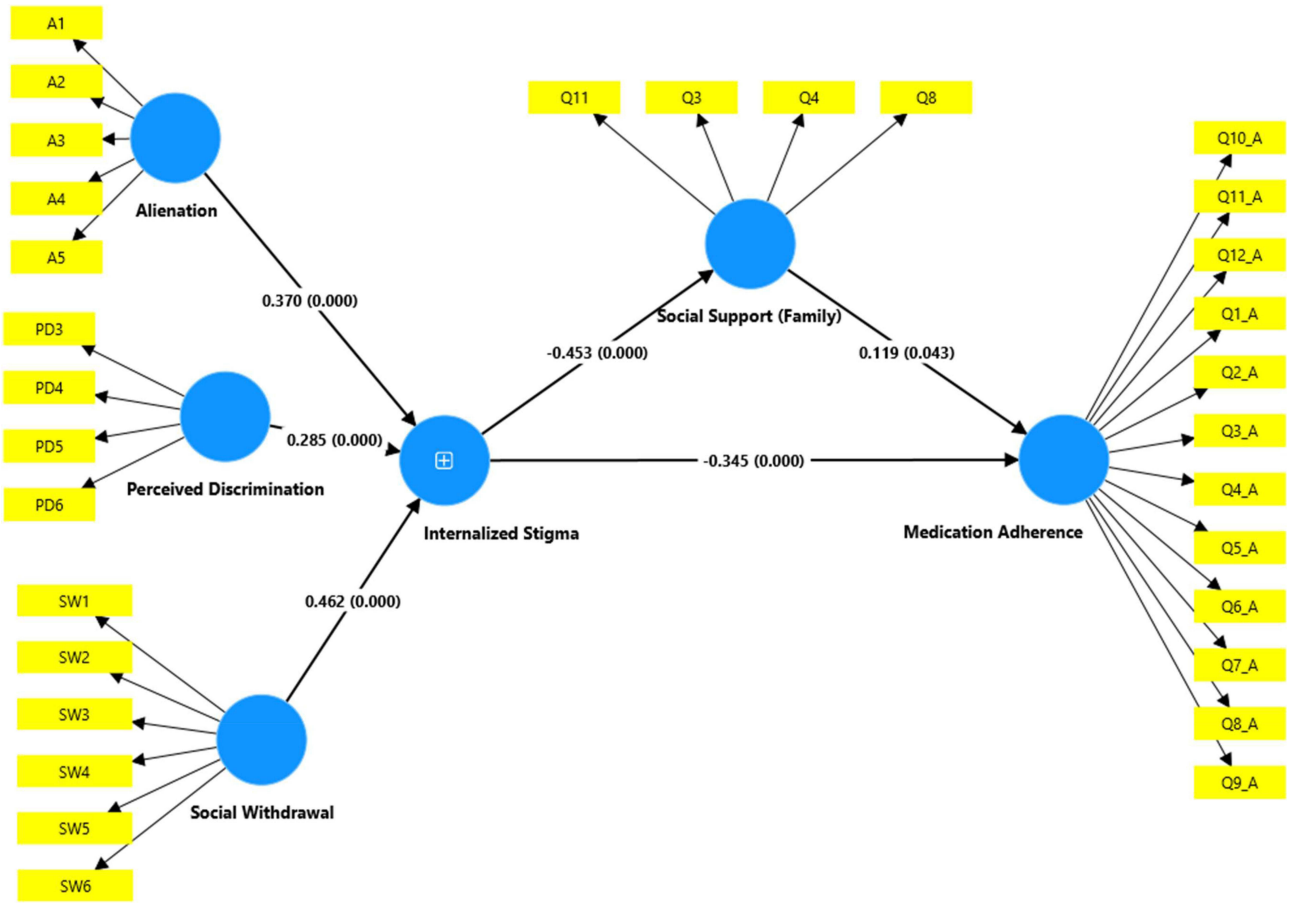

Figure 1 Mediation model on the effect of family support in the relationship between internalized stigma and medication adherence.

(item 15; 0.665) and two items from medication adherence (items 12 and 3; 0.557 and 0.686, respectively) were still lower than the cut-off score, these items were retained as they did not affect the reliability and validity of the constructs. After removing the stereotype domain, all the constructs have high composite reliability (rho_c), ranging from 0.912 to 0.951. The AVE for all constructs was acceptable, ranging from 0.552 to 0.825. The HTMT ratios between all predictors and the dependent variable were lower than 0.90, ranging from 0.280 to 0.402, indicating that discriminant validity was achieved.

All the inner VIF values were lower than 3.3; hence, common method bias and multicollinearity issues were absent in the structural model. A repeated indicator approach was used to assign alienation, perceived discrimination, and social withdrawal to the higher-order construct, which is internalized stigma. The bootstrapped mediation analysis showed that the indirect effect of family support on the relationship between alienation ($\beta = -0.020$, $t = 1.656$, $p = 0.049$), perceived discrimination ($\beta = -0.015$, $t = 1.668$, $p = 0.048$), social withdrawal ($\beta = -0.025$, $t = 1.645$, $p = 0.050$), and medication adherence were marginally significant. The adjusted R square revealed that 16.4% variance of medication adherence was explained by internalized stigma and family support. Based on the f^2 value, internalized stigma had a small effect on medication adherence ($f^2 = 0.114$), but family support showed no effect ($f^2 = 0.013$) (Figure 1).

Discussion

This study aimed to examine the prevalence and factors associated with medication adherence in patients with MDD, to contribute to limited literature on factors that may drive MDD treatment non-adherence in Malaysia. The results showed that more than half of the participants reported moderate/low medication adherence. A history of psychiatric ward

admission was significant in predicting moderate/low medication adherence. In addition, internalized stigma were risk factors, while family and others' support were protective factors against moderate/low medication adherence.

The prevalence of moderate/low medication adherence in this study was 57.1%. The prevalence found in this study was slightly higher than reported in a systematic review and meta-analysis study by Semahegn et al,[13] which showed the magnitude of psychotropic medication non-adherence among patients of MDD to be 50.0%. Another study in Nepal showed that the rate of non-adherence among the depressive patients ranged from 40 to 66.9% with antidepressants.[47] These variations may be due to a range of factors, such as differences in cultural values and health systems. For example, some Malaysians may prefer traditional medicine or religious interventions compared to taking psychotropic medications.[48]

While our study did not find a significant difference in adherence between those with and without chronic diseases, about a quarter of our participants (26.4%) reported a comorbid condition, and more than half of them (55.6%) reported low/moderate adherence. Our proportion of low/moderate adherence in patients with comorbidities was lower than the prevalence of patients with MDD and diabetes comorbidity in the US (64.1%).[49] Furthermore, a meta-analysis of studies conducted in the US found that patients with comorbid chronic diseases and MDD had 1.76 higher odds of being non-adherent than those without a comorbidity.[50] Due to the lack of supporting data, it is difficult to extrapolate on the reasons underlying our non-significant results, and therefore, further studies are needed to investigate medication adherence in patients with comorbid MDD and another chronic disease in Malaysia.

With regards to religious affiliation, our study found that Buddhists had lower odds of reporting low/moderate adherence compared to Muslims. Self-compassion is a central Buddhist tenet which encourages self-care and decreases stigma and prejudice, and may thereby decrease internalized stigma that serves as a barrier towards medication adherence.[51,52] Buddhist-based self-compassion interventions have been associated with higher treatment adherence.[53] Future studies could further investigate the mechanisms encouraging higher medication adherence among Buddhists in Malaysia.

Next, participants with psychiatric ward admission history had 3.5 times higher odds of reporting low/moderate medication adherence. The study results are consistent with the findings of Baeza-Velasco et al, who found that those with more hospital admissions had worse adherence.[54] Ward admission for MDD denotes a history of more severe psychopathology, which was associated with lower medication adherence, through mechanisms of low motivation, distractibility, executive impairment, and despair about their condition.[55] In Malaysia, higher depressive symptoms in patients with type-2 diabetes were associated with lower medication adherence.[56]

In this study, internalized stigma in general, and alienation, stereotype, discrimination, and social withdrawal, specifically, were associated with moderate/low medication adherence. The findings of this study were consistent with another study investigating the association between stigma and medication adherence in Ethiopia, in which those with higher stigma had 2.31 higher odds of nonadherence.[57] Stigma associated with perceived discrimination may influence an individual's decision to stop obtaining treatment from a health care facility in which they experience dismissal or disrespect.[58] Furthermore, alienation and social withdrawal may hinder help-seeking or treatment follow up.[59]

The results of the mediation analysis suggest that the negative effects of internalized stigma on medication adherence were partially mediated by family social support. This study is consistent with another study by Turan et al,[60] which found that internalized stigma in women living with HIV was associated with lower perceived social support (or increased loneliness), which subsequently predicted higher levels of depressive symptoms. These symptoms, in turn, were linked to suboptimal medication adherence.[60] The importance of family support in comparison with support by significant others and friends is highlighted in our study. The results are consistent with findings from a systematic review on pharmacological adherence in mental health patients, where family support was positively associated with adherence.[55] The family unit has been found in some studies to be an important source of support for patients' medical regimen, and this includes providing practical support such as providing reminders or actual assistance in taking the medication.[61] In comparison, friends and significant others may not be in the position to do so as they may live in different households. In addition, a past study in Malaysia shows that family members tend to provide lower support for taking anti-depressants (eg, discouraging the patient from taking their medication) if they held stigmatizing attitudes.[17]

Conversely, if the family held less stigma against depression and antidepressant medication, they may provide more encouragement for the patient to continue with the medication, and even provide practical support for doing so.

This study is significant for a variety of reasons. Given the significance of medication adherence in the treatment of MDD patients, it will be helpful to identify the psychological and demographic aspects linked to nonadherence so that clinicians could address them during consultation. Actions that could be immediately implemented in clinical settings based on these findings are to assess internalized stigma and family support in patients who find it challenging to adhere to their medication regimen. In addition, public health promoters and community health workers could also disseminate messages that are targeted to alleviate specific stigmatizing beliefs of depressive patients, and enhance social support for them. Family support, in particular, may be a relevant point for intervention as families have been shown to be the only source of support that was significantly related to medication adherence, and had a positive effect in attenuating the effect of internalized stigma on medication adherence.

There are several limitations to this study. First, as a cross-sectional study, we could not infer cause-and-effect in the relationship between variables. Secondly, as the data was obtained through self-administered and self-reported measures, bias may be present. Future studies could reduce this bias by corroborating patient reports with clinician assessments or objective outcomes such as pill counts. The study's focus on outpatient clinic attendees excluded those who declined treatment or required hospitalization, potentially missing a broader spectrum of experiences. We also did not collect information, during the study period, on the number of patients with MDD who attended the outpatient clinic. Single-center sampling restricts the generalizability of the findings to a larger Malaysian population. Language barriers posed limitations, as the questionnaires were offered only in Malay and English. Consequently, individuals unfamiliar with these languages, particularly those from lower educational backgrounds, were excluded from the study. From our universal recruitment method, we did not record how many participants were approached, and how many of those approached refused to join the study. Therefore, we could not determine the non-response rate of the study. Notably, two participants found the ISMI questionnaire distressing and chose not to complete it, revealing the need to anticipate participant distress and preparedness to refer them should the need arise. Future studies could consider multiple sites in both rural and urban areas to increase the generalizability of the study. In addition, the above limitations could be overcome through the study design to carry out longitudinal studies, questionnaires in other commonly spoken languages in Malaysia such as Tamil and Chinese, and to include depressed individual in community settings and inpatients.

Conclusion

In short, more than half of the participants demonstrated low to moderate medication adherence. Higher internalized stigma predicted higher odds of low/moderate medication adherence, but this effect was attenuated by family support. Therefore, internalized stigma and family support are important points of intervention for patients with MDD in the Malaysian setting.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

Permission was obtained from the Psychiatry Head of the Department and ethical approval was obtained from the Universiti Malaya Medical Research and Ethics Committee [MREC: NMRR ID: 23-0081-XAU (IIR)]. Participation was voluntary and written informed consent was obtained from participants. This study complies with the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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