ORIGINAL ARTICLE

Mixed Features Specifier in Mood Disorder: The Prevalence and Associated Factors

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ABSTRACT

Introduction: Malaysia's unique cultural landscape may influence the manifestation of mixed features differently than in global studies. We've conducted the first study on the prevalence of the Mixed Feature Specifier (MFS) in mood disorders in Malaysia, addresses crucial research gaps to potentially inform culturally sensitive treatment approaches in Malaysia. **Methods:** This cross-sectional prevalence study was conducted at a psychiatric hospital in Malaysia, using a researcher administered questionnaire, consisted of five parts which includes sociodemographic factors, clinical characteristics, MADRS score, YMRS score and QoL score. Data was analyzed using SPSS version 24.0. **Results:** 148 patients were recruited into this study. Overall prevalence of MFS among Major Mood Disorder was 29.8%. There were significant associations between ethnicity (X2=9.063; p=0.028), marital status (X2=18.738; p<0.001) and average monthly income (X2=31.534; p=<0.001) with MFS. In terms of clinical characteristics, there were significant associations between number of hospitalizations (X2=41.026; p<0.001), trials of medications (X2=29.540; p<0.001), total number of medications on (X2=42.338; p<0.001), history of ECT (X2=10.590; p=0.001), family history of mood disorder (X2=20.944; p<0.001), suicidal attempts (X2=26.570; p<0.001), history substance use (X2=19.249; p<0.001), compliance to treatment (X2=4.310; p=0.038), YMRS score (X2=16.799; p=0.001) and MADRS score (X2=43.525; p<0.001) with MFS. **Conclusion:** We identified predictors associated with MFS, such as amount of income, substance use and number of hospitalizations. Sociodemographic and clinical characteristics are significantly associated with MFS, with significant differences between the QoL of MFS and non-MFS patients. This could foster early detection of cases, hence addressing the psychological needs of both MFS and non-MFS patients.
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INTRODUCTION

The landscape of mixed states in psychiatry, explored by McIntyre et al. (2015), has undergone a transformative journey, particularly in the realm of mixed episodes[1]. For over two decades, the debate swirled around the rigid DSM-4 criteria, demanding the simultaneous presence of depressive and manic episode criteria for a mixed episode diagnosis. Recognizing the impracticality of this approach, the DSM-5 introduced a more nimble 'specifier.' This updated version requires just three symptoms from the opposite pole to diagnose depression or mania with mixed features, as highlighted by Malhi et al. (2014) [2]. Notably, the DSM-5's shift to the term "Mixed features specifier" from "mixed episode," as pointed out by Malhi and colleagues, signifies a departure that adds a dynamic twist to psychiatric diagnostics, steering away from the constraints of its predecessors.

Literature has demonstrated that approximately 40% of patients have mixed episodes, but this figure may be much higher within the context of DSM-5 [3]. The wide range of variation in the reported prevalence of mixed symptoms and behaviors in major depressive disorder (MDD), bipolar disorder (BD) mania/hypomania and BD Major Depressive Episodes (MDEs) highlights current imprecision of the 'mixed' episode concept and leaves several uncertainties [4].

Studies have found that considerable manic or mania-related symptoms were admixed during a depressive episode were more frequent amongst the bipolar depressives compared to the unipolar depressive group [5]. Evidences point out that mixed features in either Depression and (hypo)mania is linked with substantial and potentially important differences in clinical

and demographic characteristics compared to their counterpart without mixed features [6].

Literatures have persistently reported that major mood disorders such as MDD and BD with Mixed features are associated with a poorer outcome and a more complex progress of illness. Additionally, the prevalence rate across various studies varies. To date, there are no studies that examines the prevalence of mixed features in mood disorders among the Malaysian population. Conducting the first study on the prevalence of the Mixed Feature Specifier in mood disorders in Malaysia addresses crucial research gaps and holds significant importance. Malaysia's unique cultural and ethnic landscape may influence the manifestation of mixed features differently than in global studies, contributing to a more nuanced understanding of mood disorders within diverse populations. This research has the potential to inform culturally sensitive treatment approaches, guide public health planning, and enhance mental health services in Malaysia.

A better knowledge on this phenomenon can provide early detection among these group of patients, also to assist clinicians to understand the complexities of the course. Moreover, a timely and a more appropriate clinical measures could be provided to improve the disease prognosis.

MATERIALS AND METHODS

Study Design

This cross-sectional study was conducted at the outpatient Psychiatric Clinic of Hospital Bahagia Ulu Kinta, the oldest and largest Psychiatric Hospital with 1800-bed in Malaysia. The study relied upon convenient sampling after obtaining written informed consent due to limited resources and time constraints.

This study examined the prevalence of Mixed Feature Specifiers in MDD, BD mania/hypomania and BD MDEs and its associating factors with regards to socio-demographic factors, symptoms severity, and quality of life among the respondents.Criteria for inclusion were participants who were diagnosed with Major Depressive Disorder or Bipolar Disorder using DSM-5 by psychiatrist, participants within 18 to 60 years old and were able to converse and comprehend in either Bahasa Melayu or English. Patients with serious underlying medical condition, has another major psychiatric illness, or were too disturbed were excluded from participation.

Study approval was obtained from the Medical Research & Ethics Committee (MREC) of the Ministry of Health (MOH), Malaysia (reference: NMRR-19-4008-52206(IIR)) and by the Research and Ethics Committee, University Malaya Medical Centre (UMMC).

Study Population

The sampling population consisted of patients who were diagnosed by a board psychiatrist with MDD, BD mania/hypomania and BD MDE based on DSM-5 criteria who visited the Outpatient clinic during the study period, in Hospital Bahagia Ulu Kinta, This study

This group of patients who fulfil the specifier criteria within DSM-5 will be recruited and further evaluated for MFS. Subjects were excluded if they have serious medical condition, comorbid of another major psychiatric disorder, or with severe intellectual disability or disorganized or non-cooperative.

The sample size calculation was performed using the formula derived from Ziegel et al. and referenced the prevalence to a study done by Miller et. al. in 2016 [7, 8].

Procedure

The authors administered questionnaires consisted of five parts: sociodemographic factors, clinical characteristics, Montgomery-Asberg depression rating scale (MADRS) score, the Young mania rating scale (YMRS) score and quality of life (QoL) score, to all eligible recruited participants (Fig. 1). All questionnaires were validated with consistent Alpha Cronbach values of >0.5. The Malay version of WHOQOL-BREF was locally validated by Hasanah et al. (2003) [9]. A fair to good test-retest reliability was obtained for each item in the scale, with intra class correlation coefficient range from 0.49-0.88. The original English version was used and translated to Malay Language during administration. All instruments used in this study have been validated.

Data Analysis

Data analysis was conducted with the Statistical Package for the Social Sciences, Windows version 24 (SPSS Inc.,

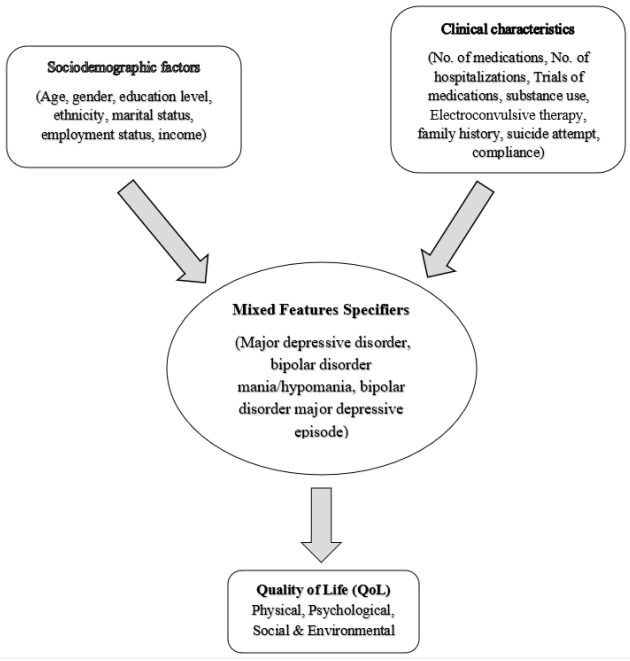

Figure 1: Conceptual Framework of Study

Chicago [IL], US). The normality of the data distribution was assessed by normality test using Kolmogorov-Smirnov. All p-values were considered statistically significant with p<0.05, at 95% confidence interval (CI). Association between two categorical variables was analyzed using Chi-square test (χ^2), Fisher's exact test was used when more than 20% of cells have expected count of less than 5. The predictors of MFS were analyzed using binary logistic regression (BLR) analysis.

RESULTS

Sample Recruitment

A total of 148 subjects, who presented to BUKH and diagnosed with MDD or BD during the recruitment period, were eligible for the study, as per sample size calculation.

Prevalence of Mixed Feature Specifiers Among Mood Disorder Patients

The overall prevalence of MFS among Major Mood Disorder was 29.8%. Individually, the prevalence of MDD without MFS in this study was 46.6% while MDD with MFS was 16.2%.

Prevalence of BD mania/hypomania without MFS was 13.5% while BD mania/hypomania patients with MFS was 8.1%. Prevalence of BD MDE without MFS was 10.1% while BD MDE with MFS was 5.5%.

Sociodemographic profile and Clinical Characteristics

The median age of respondents was 34-year-old. Both male and female genders were almost equally distributed (50.7% and 49.3% respectively). Ethnicity wise, 54% and 52.0% are from the Malay and Chinese ethnic group respectively. The majority (85%) were married and 90.5% had completed only up to secondary. Two thirds of respondents were employed, with over half of respondents earn below RM1000 monthly (60.8%).

Eighty-nine (60.1%) subjects have family history of mood disorder, 56.1% had 2 or less hospitalization and majority (59.5%) of respondents had more than 2 trials of medications, with 43.2% on single medication, 38.5% on double medications and 18.2% on triple medications. In terms of history of electroconvulsive therapy (ECT), 93.9% of respondents had not been subjected to ECT. Majority (75.7%) reported no history of suicidal attempt and 72.3% had no history of substance use. Ninety-nine (66.9%) of respondents exhibited good compliance to medications and treatment. Most of the respondents (71.6%) had a YMRS score of being in remission whereas for MADRS scoring, 34.5% was asymptomatic and 48.0% had mild depression.

Association between Socio-demographic Factors and Clinical Characteristics with MFS

The association between socio-demographic factors are depicted in shown in Table I. There were significant associations between ethnicity (X2=9.063; df 1; p=0.028), marital status (X2=18.738; df 1; p<0.001) and average monthly income (X2=31.534; df 1; p=<0.001) with MFS.

Table I: Association between socio-demographic factors with MFS

Socio demographic	MFS		X^2	df	P*
	Yes n (%)	No n (%)			
Age group			0.675	1	0.714
≤30	10 (33.3)	20 (66.7)			
>30	34 (28.8)	84 (71.2)			
Gender			0.543	1	0.073
Male	30 (40.0)	45 (60.0)			
Female	45 (61.6)	33 (38.4)			
Ethnicity			9.063	1	0.028
Malay	21 (38.9)	33 (61.1)			
Non-Malay	23 (24.5)	71 (75.5)			
Marital Status			18.738	1	< 0.001
Single/Divorced/ Widowed	25 (35.7)	45 (64.3)			
Married	19 (24.4)	59 (75.6)			
Education level			0.265	1	0.607
Up to Secondary	39 (29.1)	95 (70.9)			
Higher than secondary	5 (35.7)	9 (64.3)			
Employment			0.753	1	0.564
Employed	21 (21.2)	78 (78.8)			
Not employed	23 (46.9)	26 (53.1)			
Average income			31.534	1	< 0.001
<1000	42 (46.7)	48 (53.3)			
>1000	2 (3.4)	56 (96.6)			

* Categorical data were analysed by Chi-square test or Fisher's exact test. Others are continuous data analysed by independent-samples t test.

The association between clinical characteristics and MFS is shown in Table II. There were significant associations between number of hospitalizations (X2=41.026; df 1; p<0.001), trials of medications (X2=29.540; df 1; p<0.001), total number of medications on (X2=42.338; df 1; p<0.001), history of ECT (X2=10.590; df 1; p=0.001), family history of mood disorder (X2=20.944; df 1; p<0.001), suicidal attempts (X2=26.570; df 1; p<0.001), history substance use (X2=19.249; df 1; p<0.001), compliance to treatment (X2=4.310; df 1; p=0.038), YMRS score (X2=16.799; df 1; p=0.001) and MADRS score (X2=43.525; df 1; p<0.001) with MFS.

Sociodemographic and Clinical Characteristics Predictors of MFS

Binary logistic regression (BLR) was used to predict the 3 sociodemographic factors of MFS, namely ethnicity, marital status and income, as these 3 factors returned a significant association when tested with Chi-square test (Table III). All the variables were analyzed using 'ENTER', 'Forward-WALD' and 'Backward-WALD'. The 'ENTER' method was selected as it produced the most number of significant predictors. There was no collinearity. MFS patients are 4.1% less likely to be earning an income of >RM1000 (AOR=0.041, 95% CI=0.009-0.181).

Table II: Association between clinical characteristics with MFS

Medical history	MFS		X^2	df	P*
	Yes n (%)	No N (%)			
No. of hospitalization			41.026	1	<0.001
2 or less	7 (8.4)	76 (91.6)			
>2	37 (56.9)	28 (43.1)			
Trials of medication			29.540	1	<0.001
2 or less	3 (5.0)	57 (95.0)			
>2	41 (46.6)	47 (53.4)			
No. of medication			42.338	1	<0.001
2 or less	22 (50.0)	99 (81.8)			
>2	22(50.0)	5 (18.5)			
H/O ECT			10.590	1	0.001
Yes	7 (77.8)	2 (22.2)			
No	37 (26.6)	102 (73.4)			
Family h/o mood disorder			20.944	1	<0.001
Yes	30 (50.8)	29 (49.2)			
No	14 (15.7)	75 (84.3)			
Suicidal Attempts			26.570	1	<0.001
Yes	23 (63.9)	13 (36.1)			
No	21 (18.8)	91 (81.3)			
Substance use			19.249	1	<0.001
Yes	23 (56.1)	18 (43.9)			
No	21 (20.0)	86 (80.0)			
Compliance			4.310	1	0.038
Good	24 (24.2)	75 (75.8)			
Poor	20 (40.8)	29 (59.2)			
YMRS			16.799	3	0.001
Remission	25 (23.6)	81 (76.4)			
Minimal symptoms	13 (36.1)	23 (63.9)			
Mild mania	3 (100)	0 (0)			
Moderate mania	3 (100)	0 (0)			
MDRS			43.525	3	<0.001
Asymptomatic	1 (2.0)	50 (98.0)			
Mild depression	24 (33.8)	47 (66.2)			
Moderate depression	17 (70.8)	7 (29.2)			
Severe depression	2 (100)	0 (0)			

Abbreviations: ECT = Electroconvulsive therapy; YMRS – Young Mania Rating Scale; MADRS - Montgomery–Asberg Depression Rating Scale.
* Categorical data were analysed by Chi-square test or Fisher's exact test. Others are continuous data analysed by independent-samples t test.

BLR was again used to predict the clinical characteristics of MFS (Table III). The odds of MFS patients with more than 2 hospitalizations are 18.5 times higher than in patients with less than 2 hospitalizations (AOR=18.487, 95%CI=4.573-74.735). Patients with MFS are 18.3% less likely to have had no history of substance use if compared to patients without MFS patients (AOR=0.183, 95%CI=0.046-0.726).

Quality of life (QoL) among respondents with MD

Table IVa compares the mean scores of all 4 domains for QoL between MDD and MDD MFS. Mann-Whitney U test was performed to assess the differences between mean scores and results shows that all 4 domains have significant differences between the mean scores in respondents with MDD and respondents with MDD MFS.

Table IVb shows the comparison between the means scores of all 4 domains for QoL between BD mania/hypomania and BD mania/hypomania. Mann-Whitney U test was performed, and all 4 domains have significant differences between the mean scores in respondents with BD mania/hypomania and respondents with BD mania/hypomania MFS.

The comparison between the means scores of all 4 domains for QoL between BD MDE and BD MDE MFS is shown in Table IVc. Mann-Whitney U test was performed and all 4 domains have significant differences between the mean scores in respondents with BD MDE and BD MDE MFS.

DISCUSSION

Prevalence of Mixed feature specifier (MFS)

In this study, we reported the point prevalence of MDD MFS among MDD patients as 25.8% among our 148 recruited respondents, which was much higher than that reported by Shim et. al. (approximately 6.5%) [10]. However, the sample population and methodology employed by Shim and colleagues focused on inpatient sample and a retrospective history obtained from chart review. The possibility of reviewer bias could have been present as there were no structured interview used.

In the context of BD, we demonstrated the point

Table III: Sociodemographic and clinical characteristics predictors of MFS (ENTER Method)

Factors	B	SE	Wald	df	p	AOR	95% CI	
							Lower	Upper
Ethnicity								
Malay						1		
Non-Malay	-0.640	0.439	2.119	1	0.145	0.528	0.223	1.248
Marital Status								
Single/Divorced/Widowed						1		
Married	-0.191	0.431	0.197	1	0.657	0.826	0.355	1.922
Income								
≤1000						1		
>1000	-3.188	0.754	17.880	1	<0.001	0.041	0.009	0.181
No of hospitalizations								
≤ 2						1		
> 2	2.917	0.713	16.752	1	<0.001	18.487	4.573	74.735
No of Medications trials								
≤ 2						1		
> 2	21.946	4185.5	0.001	1	0.996	33975	0.001	-
Substance use								
Yes						1		
No	-1.700	0.704	5.831	1	0.016	0.183	0.046	0.726
Suicidal Attempt								
Yes						1		
No	-0.084	0.756	0.012	1	0.911	0.919	0.209	4.047
ECT								
Yes						1		
No	-19.966	4185.46	0.001	1	0.996	0.001	-	-

Abbreviation: ECT= Electroconvulsive therapy.
1 = Reference group

Table IVa: QoL differences between MD with MFS and non-MFS

Domain	Group, Mean (SD)		Test	Value	p-value
	MDD	MDD MFS			
Physical	62.32 (7.518)	48.04 (6.147)	*U*	9.229	<0.001
Social	61.54 (8.010)	50.54 (8.251)	*U*	5.665	<0.001
Psychological	59.20 (8.588)	36.67 (9.379)	*U*	10.357	<0.001
Environmental	60.55 (9.995)	46.50 (3.022)	*U*	10.392	<0.001

Table IVb: QoL differences between BD mania/hypomania with MFS and non-MFS

Domain	Group, Mean (SD)		Test	Value	p-value
	BPD mania/ hypo	BPD mania/ hypo MFS			
Physical	56.00 (10.285)	48.00 (4.671)	*U*	3.001	0.006
Social	55.25 (10.109)	47.50 (4.758)	*U*	2.930	0.007
Psychological	45.25 (14.980)	29.58 (5.435)	*U*	4.235	<0.001
Environmental	52.10 (9.994)	45.50 (4.523)	*U*	2.550	0.016

Table IVc: QoL differences between BPD II with MFS and non-MFS

Domain	Group, Mean (SD)		Test	Value	p-value
	BD MDE	BD MDE MFS			
Physical	62.27 (7.035)	47.00 (3.207)	*U*	7.129	<0.001
Social	62.27 (7.787)	46.25 (3.105)	*U*	6.992	<0.001
Psychological	52.07 (11.823)	32.75 (7.421)	*U*	4.799	<0.001
Environmental	63.93 (7.304)	45.50 (5.318)	*U*	6.922	<0.001

Abbreviations: BD = Bipolar Disorder; MDE = Major Depressive Disorder; MFS = Mixed Features Specifiers

prevalence of MFS among BD mania/hypomania patients and MFS among BD MDE patients, as 37.5% and 34.8%, respectively. The overall prevalence of bipolar patients diagnosed with mixed features across literatures around the world were approximately 40% since 1970s till recently [11-13]. The prevalence rate of MFS across both mood states in bipolar disorder in this study, corresponds to the prevalence obtained by McIntyre and colleagues within the Canadian population, as 39.4% of MDE patients had MFS, while 37.8% of patients with hypo/mania had MFS [1].

Although the small sample size posits as a limitation, the prevalence could be generalized when the data is taken alongside with comparable evidence in other studies. This study hence provides an indirect inference that MFS remains underdiagnosed as some symptoms overlaps and most of the symptoms present are subjective.

Sociodemographic factors of MFS

Ethnicity and Marital status

In this study, we reported a significant association of MFS with the Malay ethnic (38.9%), (p=0.028). This result could be in part attributed to the lower socioeconomic status and higher unemployment rate among the Malay ethnicity, which explains the higher symptom severity. [14]. Hence, the small sample size and methodological limitation could have contributed to the higher prevalence of MFS within the Malay ethnic.

Among the respondents who were diagnosed as MFS, 35.7% were either single, divorced or widowed. There was significant association between marital status (p<0.001) with MFS, in concord with similar studies conducted globally which showed that higher likelihood of MFS to be either single, separated or divorced [1, 6].

Employment status and Income

Mood disorders has been highly associated with increased rates of job related difficulties and unemployment, about 60% of this patient group are unemployed while about 90% of them suffers from job related difficulties [15]. In this study however, majority of the respondents were employed as opposed to the findings of most studies [16-18]. This result corresponds to a previous local study Taha and Colleagues which found about 59.7% and 4.1% of patients with depressive disorder were employed in a full time and part-time job, respectively [19]. The difference in results could be attributed to the sample population which is from the outpatient cohort where most symptoms are remitted. Arguably, employment status directly affects the income source, whereby we observed significant association between average monthly income (p=<0.001) with MFS. MFS patients are 4.1% less likely to be earning an income of >RM1000 (AOR=0.041), in concordance with the findings of Tondo and McIntyre [1].

Clinical characteristics of MFS

Familial History of MD

Majority, 89 (60.1%) of respondents has a family history of MD. Among the respondents with MFS, 50.8% has family history of MD. In concordance to a Korean retrospective cohort study, that MFS regardless of the episode showed a correlation with both types of MD [3]. Similarly, a large population database study revealed that parental diagnosis of BD and parental depression with psychosis are important predictors for the switch incidences from unipolar depression to BD. Hence, family history of MD could be a significant predictor, and a red flag sign for MFS in both MDD and BD [20].

Number of Hospitalizations, Pharmacological Therapy and Medications Combination

There were significant associations between number of hospitalizations (p<0.001) with MFS, with the odds of MFS patients having over 2 hospitalizations are 18.5 times higher than in patients with less than 2 hospitalizations. A retrospective study of patients with BD and Unipolar Major depression found that BD patient were four times more likely to have been admitted to the hospital over the previous 6 months [21]. The increased number of hospitalizations reflects on acute mood state and symptoms severity that leads to higher economic burden for the patient, and their families [22].

Increased failure of medication has higher negative implications to the patient in terms of treatment adherence, negative attitude towards treatment which is seemingly another major burden among BD patients. Goldberg et al (2009) examined at the prevalence of polypharmacy across different mood states within BD and found that 81% from the total sample received complex polypharmacy , among which 53% of the respondent were taking non-psychiatric medications. From these total sample the depressed state receiving complex polypharmacy was 37%, Manic state 42% while the mixed state were 19%.[23]. Complex polypharmacy in this study was defined as 4 or more medications. Therefore, a significant association between number of previously tried medications among patients with MDD or BD, should provide a high index of suspicion of MFS. This study further examined the number of medications. Among the respondents who were with MFS, 50% are on >2 medications, with significant associations ($p<0.001$) with MFS.

The use of Electroconvulsive therapy (ECT) and Suicidal Attempts

Among the respondents who were with MFS, 77.8% had history of ECT. There were significant associations between history of ECT with MFS and these findings correspond with the findings obtained by other international studies [11, 24].

There are well established evidence showing strong association between suicidal risk factors and mixed symptoms. A study by Song and colleagues, highlights that mixed episodes strongly predicts suicide attempts alongside with a study by Valtonen.[25, 26] Although, the rates of suicidal attempts in MFS in this study is not an accurate representative of the Malaysian population, the significant association found in this study warrants deeper exploration and a more thorough assessment for suicide risk factor during clinical practice.

Substance Use, Compliance to Medications and Treatment

Substance use commonly occur among psychiatric disorders especially in MD. In this study, majority of patients reported an absent history of substance abuse (72.3%). This finding contradicts many other studies that has a converging result that point out strong associations of mood disorder with substance abuse. This discrepancy could be possibly due to reporting or recall biases. The histories obtained were mostly from the account of patient and the records, which could have been concealed or missed.

Medication compliance could affect the outcome and severity of an illness. In this study, there were significant associations between compliance to treatment ($p=0.038$) with MFS, where 40.8% of patients with MFS had poor compliance to treatment. This finding is in line with the EMBLEM study and other studies that showed high prevalence of poor compliances among patients with mixed symptoms [27, 28]. Despite a significant positive correlation, the data was obtained from a self-reporting manner from the patients themselves, which could be underreported. Nevertheless, our results demonstrated that medication adherence is strongly associated with MFS among mood disorders, which could further implicate in treatment and patient outcome.

YMRS score and MADRS Scores

Hereby, we presented significant associations between the YMRS and MARDS score with MFS. Our results concur with McIntyre and Miller's findings, who demonstrated higher YMRS scores among MFS especially in depressive episode [1, 7]. These findings were similar also for MADRS scoring. This study as well as the findings of few other studies globally shows a lesser remission rate associated MFS. This is reliable indicator to a poor outcome associated with MFS.

Quality of life (QoL) in Respondents with MFS

In this study, there were significant differences between the mean scores in respondents with MDD and respondents with MDD MFS, as well as BD MFS and BD without MFS in all 4 domains: physical, social, psychological, and environmental. These domains correspond to the definition of QoL which takes into consideration of an individual's performance in daily activities such as work, play, relationship and health [29]. Our findings corresponds to Vojta et al.'s findings, whereby dysphoric mania, as this study identifies manic episodes, with concurrent presence of depressive symptoms showed lower mean scores in terms of QoL among the mixed symptoms group [30].

Gazalle and colleagues have demonstrated that there is significant impairment in social domains of the WHOQOL in patients with higher YMRS score [31]. Our study results has demonstrated that, apart from depression or depressive episode that has high predictor of poor QoL and outcome, patients experiencing MFS has comparable impairment and disability, with poorer quality of life across all domains.

Limitations and Future Research Directions

The design of this study is cross-sectional. Therefore, the causal relationship between MFS in mood disorder could not be ascertained with the associating factors as this study design only demonstrates the significance between the associated variables.

The sample population is recruited from a single site, hence the catchment area, may not be a well-represented sample to infer to the general population within the countries due to the variation of sociodemographic factors. In addition, the sample population consisted of stable outpatient patients with more respondents in remission stage.

Reporting bias could be present, as respondents who had to give accounts of substance usage, personal information of demographics such as wage, may be prone to underreport and may not depict the true prevalence. In addition, recall biases, where patients had to give certain information such as number of previous hospitalizations, or ECT, could skew the data as it is subjected to patient's memory.

Future studies on MFS could be designed as cohort study to allow calculation of incidence, relative risk, risk differences and attributing risk, which is more reflective over a certain period rather than a specific period as in this cross-sectional study.

CONCLUSION

In this study, we first reported the overall prevalence of MFS among major mood disorder in Malaysia as 29.8%, considering the limitations. Certain sociodemographic characteristics, for instance, ethnicity and marital status, are significantly associated with it. The course of illness and clinical characteristics too has been shown to be implicated by the presence of MFS. Significant associations are demonstrated between the presence of MFS with variables such as familial history of mood disorder, history of suicidal attempts, history of ECT, trials of medications, number of medications patients are on, number of previous hospitalizations, history of substance use and compliance to medications.

From these results, we could identify predictors associated with MFS which were significant in the sociodemographic factors and clinical characteristics such as amount of income, substance use and number of hospitalizations. We also demonstrated that the presence of MFS in mood disorder has significant negative implication in the QoL of MFS patients. We scrutinized the symptom severity as another component of associating factor, whereby MFS patients has significant associations with higher scores in YMRS and MADRS. Understanding the risk of MFS in mood disorders not only enhances diagnostic precision, it enables tailored treatment approaches and anticipation of course of illness, hence allows employment of targeted early preventive measures,

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