

Original article

Prevalence of depression and anxiety among the patients with multiple sclerosis and neuromyelitis optica spectrum disorder at King Chulalongkorn Memorial Hospital

Thanawat Sakthanakul^a, Thanin Asawavichienjinda^b, Sookjaroen Tangwongchai^{a,*}

^aDepartment of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

^bDepartment of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Background: Demyelinating disease is an inflammatory disease of the white matter in the brain and of the sheath that covers the nerves, optic nerves, and spinal cord, and its progression is often found to be continuously recurring and eventually develops into disability, stress, depression and anxiety.

Objectives: To study the prevalence and the related factors of depression and anxiety among patients with demyelinating disease.

Methods: Data were collected from a group of patients diagnosed with demyelinating disease by neurologists at the Outpatient Department, Neurology Unit, King Chulalongkorn Memorial Hospital. Depression and anxiety were assessed with the Thai Hospital Anxiety and Depression Scale (HADS). Social support, family relationships and duties, and the quality of life were assessed as independent variables. The data were analyzed for the prevalence of depression and anxiety. The univariate analysis and binary logistic regression were performed to define the related factors for depression and anxiety.

Results: A total of 82 patients were consecutively recruited, 92.7% were female, and 29.3% had depression or anxiety. Social support level, family relationships and duties, and quality of life were found to be in the moderate level. The multivariate analysis revealed that the factors related to depression or anxiety were the low to medium level of quality of life (OR_{adj} 9.17 [95% CI 2.23, 37.73]), and personal income below than 31,889 baht per month (OR_{adj} 4.74 [95% CI 1.24, 18.13]).

Conclusion: Almost one-third of subjects who were diagnosed with demyelinating disease suffered from either depression or anxiety. The related factors were the low quality of life and low income. Therefore, screening for depression and anxiety should be included as part of the caring process in order to increase the treatment effectiveness and quality of life for the patients.

Keywords: Demyelinating disease, depression, anxiety.

Demyelinating disease is an inflammatory disease of the white matter in the brain and of the sheath that covers the nerves, optic nerves, and spinal cord. ⁽¹⁾ Although the disease is rare, the disease progression is often found to be continuously recurring and might eventually develop into disability. There are two common types of demyelinating disease: multiple

sclerosis (MS) and Neuromyelitis optica spectrum disorder (NMOSD). ⁽²⁾ Specifically, MS is the most common type of demyelinating disease ⁽²⁾, and is often found in Caucasians living in warm climates, at a rate of 1 - 2 persons /100,000. While the prevalence rate in Thailand, as far as studies can confirm, is 0.203-0.402 /100,000. ⁽³⁾ Seventy percent of these patients are between the age of 20 - 40 years. However, in this study, the average age of the patients may be slightly higher as it combines both MS and NMOSD patients, and which the average age of NMOSD patients are shown to be higher. ⁽²⁾

It occurs in females slightly more than males at the proportion of 1.5 - 2:1. ⁽³⁾ Likewise, NMOSD is at

*Correspondence to: Sookjaroen Tangwongchai, Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

E-mail: sookjaroen@gmail.com

Received: January 28, 2021

Revised: March 24, 2021

Accepted: April 2, 2021

least 5-10 times more common in females than males, and is often found among young adults to elderlies, with the average age greater than that of MS patients.⁽²⁾

It is evident that both MS and NMOSD are typically common among working-age people. Since both conditions causes the patient to develop symptoms of fatigue, poor sleep quality^(5,6), as well as an increase in incidences of psychiatric disorders^(7,8), they put the patient at risk of developing potential disability which would further affect the family members whom the patients usually care for.^(4,9,10) The ensuing stress from adapting to the disease combined with the changes in biological factors of the nervous system usually cause patients to also develop depression. In addition, it is also speculated that the interferon beta drug group that are used to treat MS may have a direct effect towards depression, although no clear association has been found.⁽¹¹⁾ The treatment of demyelinating disease can last up to several years and the disease's progression may worsen the patients' condition and adversely affect their daily lives and may also cause anxiety, stress, depression, and discouragement during the treatment period.⁽¹²⁾ However, the aspects regarding depression are often not evaluated, leading to the lack of proper treatment initiated which in turn affect the patients' quality of life.⁽¹³⁻¹⁵⁾ Past researches have found that the prevalence of depression among patients diagnosed with multiple sclerosis was 30.5% higher than the general population, with a pooled mean prevalence of 30.5% for depression and 22.1% for anxiety.⁽¹⁶⁾ It was also found that inpatients diagnosed with demyelinating disease, severity of the disease was associated with the presence of anxiety and emotional disorders. An assessment of the Expanded Disability Status Scale⁽¹³⁾ also found that when demyelinating disease combined with depression and/or anxiety, it resulted in a lower quality of life for patients.⁽¹⁴⁾ A Thai study revealed the prevalence of depression and anxiety to be at 8.8% and 4.4% for patients with demyelinating disease respectively. Patients with suicidal tendency are 14.53 times more at risk of having depression, compared to those with no suicidal risk.⁽¹⁷⁾

As incidence of the disease is relatively small in Thailand, studies of depression occurring in patients with demyelinating disease are quite limited. This study was conducted to examine the prevalence and related factors of depression and anxiety in patients with demyelinating disease, and to explore the related factors for improving the quality of care and patients'

quality of life, such as the combined use of drugs with psychotherapy⁽¹⁸⁾ which should be able to help patients adjust, live, and work more harmoniously and efficiently in the society.

Materials and methods

This study is a cross-sectional descriptive study, recruiting a group of patients, aged between 18 - 80 years, who were diagnosed with MS or NMOSD by a neurologist at the outpatient clinic of Neurology Unit, King Chulalongkorn Memorial Hospital. The sample had to understand and communicate in Thai language and give consent, in order to participate in the research study. The exclusive criteria were as follows: Having severe and unstable medical or psychiatric condition, diagnosed of dementia, stroke, Parkinson's disease, intellectual disability, or substance use disorder, with the exception of cigarettes or alcohol. The sample size was calculated using the known proportional formula.⁽¹⁹⁾ The prevalence, based on the study of Boeschoten RE, *et al.*⁽¹⁵⁾, was found to be 0.305. The calculated sample size was 82 patients, with the data collection period between July 2019 to July 2020. This study has been approved by the Research Ethics Committee, the Faculty of Medicine, Chulalongkorn University (COA no.787/2020).

Instruments used in the research included a questionnaire on the patient's personal factors, history of psychiatric and physical diseases, treatment privilege, duration in which the patient has been suffering from demyelinating disease, type of drugs that was used for the treatment, and severity of the disease, modified from Expanded Disability Status Scale (EDSS). The depression and anxiety was assessed from the Thai version of the Hospital Anxiety and Depression Scale⁽²⁰⁾, which is widely recognized as an accurate tool for assessing depression in patients with demyelinating disease.⁽²¹⁾ The possible total score for depression or anxiety ranges from 0 - 21. The total score for each of depression or anxiety that is equal to or more than 8 will indicate that the patient is deemed to be afflicted with depression or anxiety. The social support aspect was assessed by utilizing the Thai version of the Social Support Questionnaire⁽²²⁾, which categorizes social support into 3 aspects: emotional, information, and resource or objects, with a total of 16 questions with possible score ranging from 16 - 80. The interpretation of the results was based on the data distribution by the use of mean scores and standard deviations to

classify the various levels of social support into low, medium and high. The assessment of the relationship and family duties was conducted through the Thai version of the Family Relationship and Functioning Questionnaire⁽²³⁾, which consists of 7 questions totaling 0 - 35 points. The quality of life was assessed by using the Thai version of the World Health Organization Quality of Life Brief - Thai: WHOQOL – BREF – THAI⁽²⁴⁾, in which the confidence level of the Cronbach's alpha coefficient tool was established to be at 0.8406, at an accuracy level of 0.6515. This is a self-rated questionnaire consisted of 26 questions classified into four aspects of the quality of life: physical health, psychological, social relationships, and the environmental factor, in addition to the other two aspects that are indicators of quality of life and overall health. The total score range is from 26 - 130 points. A range of score between 26 - 60 indicates poor quality of life, 61 - 95 points indicates a moderate quality of life, and a score of between 96 - 130 represents a good life quality.

Statistical analysis

Data analysis was performed by SPSS program for Windows version 22.0. Data were expressed as mean ± standard deviation (SD). Univariate analysis and binary logistic regression analysis were utilized to assess the relationship between related factors and depression or anxiety in patients. The results were presented as the adjusted odds ratio (OR) with 95% confidence interval (CI) with all the tests being presented as a two-tailed test with a statistical significance level of 0.05.

Results

Of the total 82 patients with diagnosis of demyelinating disease, 92.7% were female, with an

average age of 45.3 ± 13.6 years. 46.3% were married/cohabitating, 80.5% had an occupation with an average income of 31,899 ± 21,409 baht. 70.7% were found to have an education level of a bachelor's degree or higher. 8.5% and 13.4% of the sample had history of psychiatric disorders and other physical diseases, respectively. 56.1% were diagnosed with NMOSD with an average duration of illness of 9.1 ± 6.5 years. The average age of first experienced symptoms was 36.3 ± 13.3 years. 61.0% of the patients were being treated with drugs from the immunosuppressive group. 72.0% were able to walk without assistance for at least 100 meters. 13.4% experienced a visual level that was worse than 20/200.

The prevalence of depression in this sample was 13.4%, with mean Hospital Anxiety and Depression Scale (HADS) depressive subscore of 4.1 ± 3.5. Whereas 22.0% of the sample had anxiety with mean HADS anxiety sub score of 4.8 ± 3.6, 40 - 53 % of the recruited subjects had the scores of social supports, family relationship and quality of life in moderate level as shown in Table 1.

The statistically significant factors related to depression or anxiety in this study were low monthly personal income, having a history of psychiatric disorders, low to moderate level of quality of life and family relationships and duties as displayed on Table 2.

The multivariate analysis revealed 2 factors that predicted the risk of depression or anxiety in the binary logistic regression model, including a monthly income of less than 31,899 baht [OR_{adj.} 4.7 (95% CI 1.2, 18.1)] and low to moderate level of quality of life [OR_{adj.} 9.2 (95% CI 2.2, 37.7)] (Table 3).

Table 1. The assessment of depression and anxiety, social support, family relationships and duties, and quality of life among patients diagnosed with demyelinating disease.

	n (%)	Mean ± SD	Level n (%)		
			High	Moderate	Low
Depression	11 (13.4)	4.1 ± 3.5			
Anxiety	18 (22.0)	4.8 ± 3.6			
Depression and anxiety	5 (6.1)				
Depression or anxiety	24 (29.3)				
Social support		61.6 ± 12.0	27 (32.9)	33 (40.2)	22 (26.8)
Family relationships and duties		29.8 ± 4.6	25 (30.5)	37 (45.1)	20 (24.4)
Quality of life		93.5 ± 15.9	37 (45.1)	44 (53.7)	1 (1.2)

Table 2. The relationship between personal factors, social support, family relationships and duties, and quality of life, and depression among patients diagnosed with demyelinating disease.

	Total n = 82 (%)	Display depression or anxiety n = 24 (%)	No symptoms of depression or anxiety n = 58 (%)	P - value
Gender				
Female	76 (92.7)	22 (28.9)	54 (71.1)	1.0 ^f
Age (years)				
<45	41 (50.0)	14 (34.1)	27 (65.9)	0.332 ^c
Marital status				
Single/married/cohabitation	73 (89.0)	19 (26.0)	54 (74.0)	0.114 ^f
widowed/divorced	9 (11.0)	5 (55.6)	4 (44.4)	
Profession				
Unemployed monthly personal income (baht) (n = 67)	16 (19.5)	6 (37.5)	10 (62.5)	0.541 ^f
Mean ± SD	31,899 ± 21,409			
< 31,889 baht	39 (58.2)	16 (41.0)	23 (59.0)	0.018 ^{c*}
≥ 31,889 baht	28 (41.8)	4 (14.3)	24 (85.7)	
Education level				
Below undergraduate	24 (29.3)	8 (33.3)	16 (66.7)	0.603 ^c
Undergraduate or higher	58 (70.7)	16 (27.6)	42 (72.4)	
History of psychiatric disorders	7 (8.5)	5 (71.4)	2 (28.6)	0.021 ^{f*}
Other medical comorbidities	11 (13.4)	2 (18.2)	9 (81.8)	0.495 ^f
Type of demyelinating disease				
MS	36 (43.9)	11 (30.6)	25 (69.4)	0.821 ^c
NMOSD	46 (56.1)	13 (28.3)	33 (71.7)	
Duration that the patient has been suffering from demyelinating disease (years)				
Mean ± SD	9.1 ± 6.5			
≥ 9 years	39 (47.6)	13 (33.3)	26 (66.7)	0.441 ^c
Age that first onset (years)				
Mean ± SD	36.3 ± 13.3			
≥ 36 years	40 (48.8)	10 (25.0)	30 (75.0)	0.407 ^c
Type of drugs used in treating demyelinating disease				
No medication	21 (25.6)	8 (38.1)	13 (61.9)	0.303 ^c
Betaferon/rebif	5 (6.1)	1 (20.0)	4 (80.0)	1.0 ^f
Immunosuppressives	50 (61.0)	12 (24.0)	38 (76.0)	0.19 ^c
IVIg	6 (7.3)	3 (50.0)	3 (50.0)	0.352 ^f
Ability to walk without the assistance for at least 100 meters	59 (72.0)	19 (32.2)	40 (67.8)	0.349 ^c
Visual level that is worse than 20/200	11 (13.4)	4 (36.4)	7 (63.6)	0.723 ^f
Support from society				
Moderate/low	55 (67.1)	19 (34.5)	36 (65.5)	0.134 ^c
Family relationships and duties				
High	25 (30.5)	3 (12.0)	22 (88.0)	0.023 ^{c*}
Moderate/low	57 (69.5)	21 (36.8)	36 (63.2)	
Quality of life				
High	37 (45.1)	4 (10.8)	33 (89.2)	0.001 ^{c*}
Moderate/low	45 (54.9)	20 (44.4)	25 (55.6)	

MS: Multiple sclerosis, NMOSD: Neuromyelitis optica spectrum disorder, VIG: Intravenous immunoglobulin, SD: Standard deviation

Data analysis conducted through the use of Chi-square test (c) / Fisher exact test (f) *($P < 0.05$).

Table 3. Univariate and multivariate analysis.

	Multivariate Analysis	
	Crude OR [95%CI]	Adjusted OR [95%CI]
Monthly personal income		
< 31,889 baht (ref: ≥ 31,889 baht)	4.2 [1.2, 14.4]*	4.7 [1.2, 18.1]*
Have a history of psychiatric disorders		
Yes (ref: no)	7.4 [1.3, 41.2]*	
Family relationships and duties		
Moderate/low (ref: high)	4.3 [1.1, 16.0]*	
Quality of life		
Moderate/low (ref: high)	6.6 [2.0, 21.8]*	9.2 [2.2, 37.7]*

Data analysis conducted through the use of binary logistic regression (Forward Likelihood ratio method) *($P < 0.05$).

Discussion

From this study, it was found that 13.4% and 22.0% of patients at King Chulalongkorn Memorial Hospital who were diagnosed with demyelinating disease were afflicted with depression and anxiety disorders respectively. The percentage was less than other previous studies which reported the prevalence of depression and anxiety of 30.5% and 22.1% respectively.⁽¹⁶⁾ Our report is consistent with a study conducted by Shin JS, *et al.*⁽²⁵⁾ which compared psychiatric symptoms among MS and NMOSD patients. The study concluded that MS patients displayed symptoms of depression, anxiety, and other psychiatric conditions, at rates that were higher than NMOSD patients, as well as a lower quality of life. Another study also concluded that all MS patients should be assessed for psychiatric comorbidities in order to find appropriate mitigation measures.⁽¹³⁾ Furthermore, this study found that factors contributed to depression or anxiety were low monthly income, history of psychiatric disorders, low to moderate level of family relationships and duties, and low to moderate level of quality of life.

The factor with regards to monthly personal income has a direct effect on depression or anxiety. This may be due to the fact that the patient is unable to work efficiently, thus results in a lower income that is inconsistent with their increased expenses, which includes an increase in medical expenses. In this research, it was found that 75.0% of the patients who did not work had incomes that were below the average rate. Problems arise when these patients do not have social support which may directly affect their emotions, thoughts, feelings, and daily lives. The finding that 75.0% of the patients who were unemployed and had incomes below the average rate is consistent with a study conducted by Weich S, *et al.*⁽²⁶⁾ which examined

the relationship between income disparities and psychiatric disorders in Britain. The study found that the relationship depended on the low level of income, wide income inequality is directly linked to a greater chance of developing a psychiatric disorder. This is also consistent with the study conducted by Wongpoom T, *et al.*⁽²⁷⁾, which found that the significantly related factors included divorce or separations, regular alcohol consumption, unresolved grief, dissatisfaction of their health, insomnia, and income insufficiency. The report from Caron J, *et al.*⁽²⁸⁾, that investigated the prevalence of psychological distress and psychiatric disorders in Canada, compared samples between low and normal income groups, revealed that the rates of psychological distress and psychiatric disorders and substance abuse were much higher among low income groups.

Upon analysis of the history of psychiatric disorder factor, it was found that patients who had a history of psychiatric disorders, were at risk of either depression or anxiety. This is due to the fact that psychiatric patients are often besotted with a cognitive disorder causing an effect on their daily lives. This can lead to depression or anxiety, which is in line with the study conducted by Yaiyong O, *et al.*⁽²⁹⁾, which studied depression and sadness from the loss of an elderly. It was found that factors that were related to depression include age, marital status of being single, widowed, divorced, being uneducated, unemployed, not earning an income or earning an income less than 5,000 baht per month, or not receiving an income from their occupation, inadequate financial status of their family, not directly owning their own residences, not living with their spouse, living alone, congenital disease, having physical diseases, having a history of psychiatric disorders, the unexpected loss of someone close, and poor family relationships and duties.

When considering the subsequent factors, it was found that patients with demyelinating disease at King Chulalongkorn Memorial Hospital also had factors regarding family relationship and duties that can influence depression or anxiety. However, problems within the family are common—as every family may have potential conflicts between each member of the household. Those who face family problems may suffer from stress, headaches, frustrations, separations, work inefficiency, insomnia, mood swings, depression, despair, substance dependency, and may often fight among family members. Problems that occur may be extensive or chronic and can lead towards depression or anxiety. The lack of interpersonal relations and proper support can increase the risk of psychiatric disorders, especially depression. This is consistent with the concepts of Weissman MM, *et al.*⁽³⁰⁾, who found that the four interpersonal problems, if it can be corrected, the symptoms of depression would then be resolved. In addition, this is also consistent with the study conducted by Jitaree B.⁽³¹⁾ which revealed that the perception of the severity of the illness, the ability to perform daily tasks, and family relationships were significantly associated with depression. It was also made evidently that the severity of the illness, the ability to perform daily tasks, and family relationships, could be collaboratively used to predict depression in the elderly at a level of 31.9%.

In respect of the quality of life, we found that it had an effect on depression or anxiety. This is due to the fact that the overall quality of life directly affects how the patient lives their lives, their feelings, and how they live in society. This is consistent with the concept given by. Prinsie JC, *et al.*⁽³²⁾ in their study named, “The Effects of Depression and Anxiety on Quality of Life in Five Common Neurological Disorders”. The results of their study showed that anxiety and depression had a larger contribution to mental health component (MCS) as compared to physical health component scores (PCS), with the exception of stroke patients. Different patterns were seen across neurological diseases, with mental health variables strongly affecting MCS in all conditions, but with a sizable contribution to PCS in migraine, MS, and stroke. In summary, anxiety and depression have varying impacts on health-related quality of life across neurological diseases. Regarding a study conducted by Hellmann-Regen J, *et al.*⁽³³⁾ on “The Depressive Syndromes in Neurological Disorders”, it can be

concluded that depressive syndromes represent common comorbidities in a number of other neurological disorders such as Parkinson’s disease, multiple sclerosis, or epilepsy, in which depression has a strong impact on both quality of life and outcome of the primary neurological disorder. According to a study conducted by Jaracz K, *et al.*⁽³⁴⁾, which was about the quality of life and social support among patients diagnosed with demyelinating disease, it was discovered that depression was the primary predictor of the quality of life. This is also in line with the results of a study by Janardhan V, *et al.*⁽³⁵⁾ who studied the quality of life in patients who were diagnosed with demyelinating disease. The study found that fatigue and depression were associated with an impaired quality of life. However, as this study is a cross-sectional descriptive study, a causal relationship cannot be clearly established. An additional limitation present in this study, is that the population sample was gathered from patients at King Chulalongkorn Memorial Hospital, which is a tertiary care setting, resulting in a higher income and education level when compared to most of the country’s population. Considering the studies mentioned earlier, care, assistance, and close attention to the socio-economic aspects of the patient should also be provided in addition to medical treatment.

Conclusion

Almost one-third of the patients diagnosed with demyelinating disease were afflicted with depression or anxiety in neurology clinic, King Chulalongkorn Memorial Hospital. Factors that were related to depression or anxiety include low to moderate level of quality of life and a monthly income of lower than 31,889 baht per month. Therefore, regular screening should be performed for psychiatric disorders, especially depression and anxiety, among patients diagnosed with demyelinating disease, in order to reduce the risk of developing depression or anxiety with proper pharmacological and psychosocial interventions.

Acknowledgements

We would like to pass our heartfelt thanks to Assistant Professor Dr. Thana Nilchaikovit, who assisted in providing the Thai version of the Hospital Anxiety and Depression Scale (Thai HADS), Khun Orapan Lueboonthavatchai and Associate Professor Dr. Peerapon Lueboonthavatchai, who provided the

Thai version of the Social Support Assessment Form and the Family Relationship and Duties Questionnaire, Dr. Suwat Mahatnirunkul and his colleagues, who assisted in providing the Quality of Life Assessment Form by using the shortened version of the Thai version of the World Health Organization Quality of Life Indicators (WHOQOL-BREF-THAI).

Conflict of interest

The authors, hereby, declare no conflict of interest.

References

1. Jitpraphaikularn J, Prayoonwiwat N. Demyelinating Disease of the Central Nervous System, NMO type. Part 1 (Neuromyelitis optica). [Internet]. 2020 [cited 2020 Oct 28]. Available from: <https://www.si.mahidol.ac.th/sidoctor/e-pl/articledetail.asp?id=1235>
2. Apiwatanakul M. Clinical practice guidelines: Multiple sclerosis and neuromyelitis optica spectrum disorder. Bangkok: Tanapress; 2018.
3. Prayoonwiwat N, Pasokpadde P, Apiwatanakul M, Siritho S, Chantattarat C, Chaikledkaew U. Prevalence of idiopathic inflammatory demyelinating central nervous system disorder in Thailand. Pan Asian Pharmaceutical Sciences Asia 269 Committee for Treatment and Research in Multiple Sclerosis (PACTRIMS); 2013; Taiwan.
4. Department of Mental Health. Ministry of Public Health. MS Disease, The disease in which: the working age should be aware of Department of Mental Health. [Internet]. 2015 [cited 2018 Dec 20]. Available from: <https://www.dmh.go.th/news-dmh/view.asp?id=25729>
5. Shi Z, Chen H, Lian Z, Liu J, Feng H, Zhou H. Factors that impact health-related quality of life in neuromyelitis optica spectrum disorder: anxiety, disability, fatigue and depression. *J Neuroimmunol* 2016;293:54-8.
6. Siengsukon CF, Alshehri M, Aldughmi M. Self-report sleep quality combined with sleep time variability distinguishes differences in fatigue, anxiety, and depression in individuals with multiple sclerosis: A secondary analysis. *Mult Scler J Exp Transl Clin* 2018; 4:doi:10.1177/2055217318815924.
7. Brenner P, Alexanderson K, Björkenstam C, Hillert J, Jokinen J, Mittendorfer-Rutz E, et al. Psychiatric diagnoses, medication and risk for disability pension in multiple sclerosis patients; a population-based register study. *PLoS One* 2014;9:e104165.
8. Miao XH, Shi ZY, Chen HX, Zhou HY, Yang R. Anxiety and depression in patients with neuromyelitis optica. *Sichuan Da Xue Xue Bao Yi Xue Ban* 2017;48:900-4.
9. Tsivgoulis G, Triantafyllou N, Papageorgiou C, Evangelopoulos ME, Kararizou E, Sfagos C, et al. Associations of the expanded disability status scale with anxiety and depression in multiple sclerosis outpatients. *Acta Neurol Scand* 2007;115:67-72.
10. Seok JM, Cho EB, Lee HL, Cho HJ, Min JH, Lee KH, et al. Clinical characteristics of disabling attacks at onset in patients with neuromyelitis optica spectrum disorder. *J Neurol Sci* 2016;368:209-13.
11. Alba Palé L, León Caballero J, Samsó Buxareu B, Salgado Serrano P, Pérez Solà V. Systematic review of depression in patients with multiple sclerosis and its relationship to interferon β treatment. *Mult Scler Relat Disord* 2017;17:138-43.
12. Jitpraphaikularn J, Prayoonwiwat N. What Should I Do, When I am diagnosed with NMO. [Internet]. 2020 [cited 2020 Oct 28.]. Available from: https://www.si.mahidol.ac.th/siriraj_online/thai_version/Health_detail.asp?id=1282
13. Panda SP, Das RC, Srivastava K, Ratnam A, Sharma N. Psychiatric comorbidity in multiple sclerosis. *Neurol Neurochir Pol* 2018;52:704-9.
14. Marrie RA, Patten SB, Berrigan LI, Tremlett H, Wolfson C, Warren S, et al. Diagnoses of depression and anxiety versus current symptoms and quality of life in multiple sclerosis. *Int J MS Care* 2018;20:76-84.
15. Chanson JB, Zéphir H, Collongues N, Outteryck O, Blanc F, Fleury M, et al. Evaluation of health-related quality of life, fatigue and depression in neuromyelitis optica. *Eur J Neurol* 2011;18:836-41.
16. Boeschoten RE, Braamse AMJ, Beekman ATF, Cuijpers P, van Oppen P, Dekker J, et al. Prevalence of depression and anxiety in multiple sclerosis: A systematic review and meta-analysis. *J Neurol Sci* 2017;372:331-41.
17. Charoensak S, Samajarn S, Siritho S, Prayoonwiwat N. Prevalence of psychiatric disorders in patients with demyelinating disease in MS clinic Siriraj Hospital. *J Psychiatr Assoc Thai* 2012;57:175-84.
18. Patten SB, Marrie RA, Carta MG. Depression in multiple sclerosis. *Int Rev Psychiatry* 2017;29:463-72.
19. Daniel WW, Cross CL. Biostatistics: A foundation for analysis in the health sciences, 10th ed. New York: John Wiley & Sons Inc.;1995. p. 180.
20. Nilchaikovit T, Lortrakul M, Phisansuthideth U. Development of Thai version of hospital anxiety and depression scale in cancer patients. *J Psychiatr Assoc Thai* 1996;41:18-30.
21. Watson TM, Ford E, Worthington E, Lincoln NB. Validation of mood measures for people with multiple sclerosis. *Int J MS Care* 2014;16:105-9.

22. Lueboonthavatchai P, Lueboonthavatchai O. Quality of life and correlated health status and social support of schizophrenic patients' caregivers. *J Med Assoc Thai* 2006;89 Suppl 3: 13-9.
23. Lueboonthavatchai P. Prevalence and psychosocial factors of anxiety and depression in breast cancer patients. *J Med Assoc Thai* 2007;90:2164-74.
24. Mahatnirunkun S, Tantipiwattanasakun W, Pumphaisarnchai W, Wongsuwan K, Pornmanajirangkul R. Comparison of the World Health Organization Quality of life indicator for every 100 and 26 indicators Chiang Mai: Suan Prung Hospital, 1998.
25. Shin JS, Kwon YN, Choi Y, Lee JY, Lee YI, Hyun J, et al. Comparison of psychiatric disturbances in patients with multiple sclerosis and neuromyelitis optica. *Medicine (Baltimore)* 2019;98:doi:10.1097/MD.00000000000017184.
26. Weich S, Lewis G, and Jenkins SP. Income inequality and the prevalence of common mental disorders in Britain. *Br J Psychiatry* 2001;178:222-7.
27. Wongpoom T, Sukying C, Udomsubpayakul U. Prevalence of depression among the elderly in Chiang Mai province. *J Psychiatr Assoc Thai* 2011; 56:103-16.
28. Caron J, Liu A. A descriptive study of the prevalence of psychological distress and mental disorders in the Canadian population: comparison between low-income and non-low-income populations. *Chronic Dis Can* 2010;30:84-94.
29. Yaiyong O, Lueboonthavatchai P. Depression and grief of the elderly at the elderly associate in Nonthaburi Province. *J Psychiatr Assoc Thai* 2011; 56:117-28.
30. Markowitz JC, Klerman GL, Weissman M. *Comprehensive guide to interpersonal psychotherapy*. New York: Basic Books; 2000.
31. Jitaree B. The factors influencing depression among the elderly at a community in Nakhon Pathom Province. [dissertation]. Nakhon Pathom: Christian University of Thailand; 2012.
32. Prisie JC, Sajobi TT, Wang M, Patten SB, Fiest KM, Bulloch AGM, et al. Effects of depression and anxiety on quality of life in five common neurological disorders. *Gen Hosp Psychiatry* 2018;52:58-63.
33. Hellmann-Regen J, Piber D, Hinkelmann K, Gold SM, Heesen C, Spitzer C, et al. Depressive syndromes in neurological disorders. *Eur Arch Psychiatry Clin Neurosci* 2013; 263 Suppl 2:S123-36.
34. Jaracz K, Pawlak M, Górna K, Kołcz B, Wołoszyn D, Kozubski W. Quality of life and social support in patients with multiple sclerosis. *Neurol Neurochir Pol* 2010;44:358-65.
35. Janardhan V, Bakshi R. Quality of life in patients with multiple sclerosis: the impact of fatigue and depression. *J Neurol Sci* 2002;205:51-8.