THE ASSOCIATION BETWEEN CHRONIC SEVERE PAIN AND NEUROTICISM PERSONALITY TRAIT AMONG PATIENTS ON METHADONE MAINTENANCE THERAPY IN ALOR STAR, KEDAH

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ABSTRAK

Kajian mengenai kaitan antara kesakitan teruk kronik and ciri personaliti neuroticism di kalangan pesakit terapi gantian metadon di Alor Star, Kedah

Pengenalan: Gejala kesakitan kerap kali didapati di kalangan pesakit gantian metadon, dan kajian-kajian telah melaporkan kekerapan kesakitan teruk yang kronik berada pada paras 37-48.2%. Gejala tersebut telah menyebabkan ketidakselesaan, kehilangupayaan, dan turut menjejaskan kualiti hidup pesakit. Malah, ia juga menjejaskan keberkesanan rawatan ketagihan mereka, dan menimbulkan kesangsian pesakit terdahap terapi gantian metadon. Pelbagai kajian telah menunjukan kewujudan kaitan di antara ciri personaliti neuroticism dan kesakitan teruk kronik secara amnya, namun kewujudan kaitan sebegini masih tidak dibuktikan di kalangan pesakit terapi gantian metadon.

Objektif: Kajian ini bertujuan untuk menilai kekerapan kesakitan teruk kronik di kalangan pesakit terapi gantian metadon, serta mengkaji samada wujudnya kaitan antara ciri personaliti neuroticism dan kesakitan teruk kronik dalam kumpulan pesakit ini.

Metodologi: Ini merupakan kajian secara keratan rentas, di mana peserta dinilai dengan Brief Pain Inventory (BPI) bagi tahap gejala kesakitan, Big Five Inventory (BFI) untuk skor ciri personaliti neuroticism, Beck's Depression Inventory (BDI) untuk tahap gejala kemurungan, dan Beck's Anxiety Inventory (BAI) untuk tahap gejala keresahan. Saiz sampel dikira dengan mengunakan kaedah yang sesuai, dan teknik persampelan universal telah digunakan. Kajian ini telah melibatkan dua pusat terapi gantian metadon di Alor Star, Kedah.

Keputusan: Dengan menggunakan analisa statistik Multiple Logistic Regression, skor neuroticism ($p<0.001$), skor BAI ($p=0.012$) dan penggunaan ubat tahan sakit "over-the-counter" ($p=0.016$) telah didapati berkait dengan signifikannya dengan kesakitan teruk

kronik, dengan Odds Ratio masing-masing sebanyak 1.60 (95% CI 1.27, 2.12), 1.44 (95% CI 1.08, 1.93) dan 3.56 (95% CI 1.27, 10.01).

Perbincangan: Skor neuroticism didapati berkait secara positif dengan kesakitan teruk kronik di kalangan pesakit terapi gantian metadon, di mana dengan setiap peningkatan satu permarkahan skor neuroticism, pesakit mempunyai 60% lebih tinggi kebarangkalian untuk mengalami kesakitan teruk kronik.

Kata-kata kunci: *Neuroticism, chronic severe pain, methadone maintenance therapy (MMT)*

ABSTRACT (EXTENDED VERSION)

The Association between Chronic Severe Pain and Neuroticism Personality Trait among Patients on Methadone Maintenance Therapy in Alor Star, Kedah

Introduction: Pain is very commonly reported among previous heroin users on methadone maintenance therapy (MMT) with the prevalence of chronic severe pain (CSP) of 37-48.2% being reported. The symptom causes distress and disability, and adversely affect patients' quality of life, addiction treatment outcome and exacerbates their ambivalence towards MMT. In general, neuroticism personality trait has been shown by various studies to be associated with CSP, but similar association has yet been explored in MMT patients.

Objectives: Current study aim to assess the prevalence of CSP among patients on MMT, and to examine whether neuroticism is significantly associated with CSP in this group of patients.

Method: This is a cross-sectional study, utilizing validated Malay versions of Brief Pain Inventory (BPI) for pain measurement, Big Five Inventory (BFI) to measure neuroticism, Beck's Depression Inventory (BDI) for measurement of depressive symptoms, and Beck's Anxiety Inventory (BAI) for measurement of anxiety symptoms. All rating instruments mentioned are self-rated instruments. Sample size is determined using proper sample size calculation, and universal sampling method is applied for subject recruitment. Samples were collected from two MMT centres in Alor Star.

Results: By using Multiple Logistic Regression analyses, Neuroticism score ($p<0.001$), BAI score ($p<0.012$) and regular use of over-the-counter analgesics ($p<0.016$) were found to be statistically significant in association with CSP, with adjusted Odds Ratio of 1.60 (95% CI 1.27, 2.12), 1.44 (95% CI 1.08, 1.93), and 3.56 (95% CI 1.27, 10.01),

respectively. Multicollinearity was not detected. However, interaction was noted between neuroticism score and BAI score (p=0.028). Hence, the interaction was included into the analysis of fitness of final model. The fitness of this final model was confirmed using Hosmer-Lemeshow test (p=0.282), classification table (overall correctly classified percentage= 83.4%), and area under the receiver operating characteristic (ROC) curve test (87.9%). It was interesting to note that the prevalent of daily usage of kratom product was over 40% in the sample.

Discussion: Neuroticism score is positively associated with CSP among patients on MMT, whereby with every one point increment in neuroticism score, there is 60% higher odds of having CSP. Though it is tempting to conclude that high neuroticism score predict CSP development among patient on MMT, the author recognizes the limitations of current cross-sectional study design in establishing the nature of the association. Other significant associative factors are BAI score and regular use of over-the-counter analgesics. For every one point increment in BAI score, there is 44% higher odds of patient having CSP; and if an MMT patient use OTC analgesics for at least 3 times a week, the odds of having CSP is 3.6 times compared to those not using OTC regularly. The results suggest that, firstly, addressing anxiety in patient might help to improve CSP, and unaddressed anxiety in patient with chronic pain might in fact adversely affect the efficacy of chronic pain intervention and MMT outcome. Besides, the strong association between OTC analgesics usage and CSP suggested that when CSP among this group of patients was not adequately addressed, patient resorted to OTC analgesics to relieve their pain. OTC use as a way of self-medication was reported by studies to be common, and the practice actually exposes the patients to adverse drug reactions, which is avoidable. In the case of MMT, drug-to-drug interaction of methadone with OTC analgesics could be fatal. Over 40% of the study subjects reported use of kratom product daily. Though its

association with CSP was not statistically significant, its implication to our MMT patients cannot be ignored, as kratom has been increasingly reported locally, as well as globally, as an emerging illicit substance with high abuse potential.

Keywords: *Neuroticism, chronic severe pain, methadone maintenance therapy (MMT)*

CHAPTER 1: INTRODUCTION

Chronic severe pain among patients on methadone maintenance therapy and its implications

Pain is very commonly reported among previous heroin users on methadone maintenance therapy (MMT) with the prevalence of 37-61% (1-5). Chronic severe pain, on the other hand, was reported to have prevalence of 37-48.2% (2-4). These findings were rather high as compared to prevalence of 10% in general population (6).

Chronic severe pain (CSP) was reported to be highly problematic, with various implications. The implication of pain on people, specifically, patients on MMT is significant. Poorly controlled pain, especially chronic pain, has been shown to be associated with disability and distress (7), poor addiction outcome (2, 3), and poor quality of life among patients on MMT (8). Counselors also reported difficulties in helping patients on MMT with chronic pain (9). Chronic severe pain interfered with work and family life, obstructing the fulfillment of social obligation, and isolating patients from others. When undertreated, these symptoms can exacerbate patients' anxieties and ambivalence towards MMT (10).

Neuroticism personality trait and its clinical implications

Neuroticism is one of the personality trait in both the three and five factors models of personality, also widely known as the Big Three and Big Five theories, respectively (11). Traditionally, Eysenck referred to neuroticism as a trait of emotionality, specifically the tendency to arouse quickly when stimulated and to inhibit emotions slowly. Costa and McCrae defined neuroticism as a dimension of maladjustment or negative emotionality versus adjustment and emotional stability (12). Others proposed that facets and correlated adjectives that describe neuroticism are Anxiety (tense), Angry hostility (irritable), Depression (not contented), Self-consciousness (shy), Impulsiveness (moody) and Vulnerability (not self-confident) (13). There

were other slightly different definitions by other authors throughout the years, but the differences among definitions have been reconciled in the late 1990s with the consensus definition that, at its core, neuroticism is the propensity to experience negative emotions (12).

A person high on neuroticism is prone to experience chronic negative affect, psychological distress, and is at increased risk of developing psychopathology and mental illness (11, 12, 14-20).

Pertaining to pathophysiology of pain, neuroticism is being conceived as a vulnerability factor in pain perception. It lowers threshold at which pain is perceived as threatening, and at which pain catastrophizing emerges. Through structural equation modelling, a study had demonstrated that vigilance to pain is associated with heightened pain severity. Besides, it was found that pain catastrophizing and pain-related fear mediate the association between neuroticism and vigilance to pain (21).

Others even advocate that neuroticism measurement has the power to predict the development of psychopathologies (22, 23). Neuroticism is said to be the single most important risk factor in behavioural public health (11).

When pain catastrophizing and pain coping strategies among subjects on MMT were being studied, it was found that subjects in group with CSP reported higher level of pain catastrophizing compared to subjects without CSP (24, 25). Addressing pain catastrophizing and pain concern among patient on MMT is crucial as this response to pain is associated with adverse pain-related clinical outcomes (25).

Overview of potential associative factors of chronic severe pain among patients on MMT

Chronic severe pain in this unique group of patients has been shown, by various studies, to be associated with myriad of factors.

Specific to patient on MMT, significant associations were found between CSP and mental illnesses like depression and anxiety disorders (1, 2, 4, 8, 26). Depression and anxiety disorders were found to be common among this group of patients (3, 5, 27-29).

Certain studies attempted to explore the association between CSP and daily dosage of methadone being prescribed to patient, and the results were rather inconclusive (3, 5, 30). Other studies advocated that long term use of opioids, like methadone, might actually cause opioid-induced hyperalgesia, where patient become more sensitive to pain perception as compared to unexposed individual (30-32).

On the other hand, it is well reported in various studies that kratom provide analgesic effect to people who use it regularly. It exerts its analgesic effect through activity on opioid receptors (33, 34). Kratom product was reported being used as opioid substitute by local people in countries of Southeast Asia like Thailand and Malaysia (33). However its chronic use leads to dependence and withdrawal, with symptoms similar to that of opioid use (35).

Pain symptoms has been shown to be associated with chronic medical illness (1-3, 5). Besides, chronic pain following orthopedic traumatic injuries and fractures were found to be common, although the injuries reported in these studies were heterogeneous in terms of nature and severity (36-38). Treating chronic pain due to traumatic injury with opioid analgesics had been shown to worsen pain symptoms and could lead to other psychopathologies (39).

It is a global phenomenon that, as a result of intravenous drug use, majority of active intravenous drug user (IVDU) or previous IVDU have hepatitis C viral infection, and many of them also have hepatitis B virus and HIV infection (40). These infections, especially hepatitis C

virus and HIV has been suggested by some studies as a contributing factor in development of chronic pain (41-45), although another more recent study suggested otherwise (46).

From various evidences acquired so far, it is rather safe and reasonable to conclude that the determinants of chronic severe pain among MMT patients are likely to be complex.

Rationale of the study

Pain is prevalent among subjects on MMT. The symptom not only causes distress, impairment and poor quality of life, it also shown to be associated with poor outcomes (2, 3, 7, 8). The negative effects are expected to be worse if a subject is having chronic severe pain (CSP). The symptom is so common that research addressing this symptom and its associated factors is helpful in providing more information to guide treating clinician in managing the complaint effectively. In view of the prevalence of pain problems in MMT, some authors suggested to incorporate comprehensive and structured pain management program into substance abuse treatment program (2).

In order to manage pain, specifically CSP among this unique population, we need to know what factor or psychopathology that is associated to it, if not causing it. The factors considered in current study are neuroticism trait, depression and anxiety. Establishing a potential predicting factor of pain development, like neuroticism trait, can even help clinician to foresee, and hopefully detect the symptom early so that it did not progress into a more chronic, severe or protracted one (11).

Intravenous drug use has become a major global public health concern due to its association with rising of HIV/AIDS epidemic (40). Thus, Malaysian government has been paying great attention in the effort of harm reduction (47), thus the expansion of service of MMT is expected. This increase in service coverage should ideally be coupled with improvement in understanding of the problems faced by the target population so that better quality of service is provided to them, as well as the community. After-all, the eventual aim of harm reduction

program, of which MMT is part of it, is to create a better community by curbing the rise of HIV/AIDS epidemic.

Lastly, at the best knowledge of the author, up to the point of preparation of this research proposal, there has yet been a study done on CSP among MMT patient locally, especially study that taking neuroticism into consideration. Pain perception is a subjective phenomenon, thus what has been found in foreign study might not be the case locally. Thus the author believed that the study is a worthwhile pursue.

In summary, methadone maintenance therapy is an important part of harm reduction program in Malaysia (47), and chronic severe pain has been shown by various studies previously mentioned to be an important problem that might adversely affect its outcome.

CHAPTER 2: OBJECTIVES

2.1 General Objectives

- To determine the prevalence of chronic severe pain and level of neuroticism trait among subjects on methadone maintenance therapy in Alor Star, Kedah.
- To determine the association between chronic severe pain and level of neuroticism among subjects under study.

2.2 Specific Objectives

1. To determine the prevalence of chronic severe pain among subjects on methadone maintenance therapy (MMT).
2. To determine the association between chronic severe pain and socio-demographic and clinical characteristics of subjects undergoing MMT in Alor Star.
3. To determine the association between chronic severe pain and level of neuroticism among subjects undergoing MMT.

Research Hypothesis

Null Hypothesis- there is no difference in score of neuroticism between subjects with CSP and those without CSP.

Alternative Hypothesis- the score of neuroticism is higher among subjects with CSP compared to those without CSP.

CHAPTER 3: METHODOLOGY

3.1 Research Design

This is a cross-sectional study conducted in two methadone maintenance therapy centres in Alor Star. The centres are MMT clinic of Department of Psychiatry and Mental Health, Hospital Sultanah Bahiyah, Alor Star, and MMT clinic of Klinik Kesihatan Bandar Alor Star. Duration of study was from July 2016 till September 2016.

3.2 Population and Sample

Reference population: previous heroin users undergoing methadone maintenance therapy.

Source population: Subjects undergoing methadone maintenance therapy in Department of Psychiatry, Hospital Sultanah Bahiyah, Alor Star, and Klinik Kesihatan Bandar Alor Star.

Sampling Frame

Universal sampling was applied. All subjects undergoing methadone maintenance therapy who satisfied the inclusion and exclusion criteria were recruited into the study.

3.3 Inclusion and Exclusion Criteria

Inclusion criteria:

- Individual age ranged from 18 to 65 years old.
- Subjects that have been in the therapy for at least one year. This duration is specified because pain should present for at least 6 months in order to be defined as chronic. Furthermore, the subjects should be stable on adequate dose of methadone before the study is conducted on them.
- Subjects that consented for the study.

Exclusion criteria:

- Subject that unable to complete rating instruments due to poor literacy and command in Malay Language.

3.4 Sample Size Determination

For the first specific objective, the sample size was calculated using a formula to estimate a population proportion with good precision (48-50)

$$\mathbf{n= Z^2 [P(1-P)] /d^2}$$

P is the anticipated prevalence or population proportion. Estimated prevalence of CSP is taken as 37% (2, 4). Z value is set at conventional 1.96, for level of confidence of 95%.

d is the absolute precision required to calculate sample size. According to Naing and colleagues, it is appropriate to have a precision of 5% (to be expressed as d=0.05) if the prevalence is expected to fall between 10%-90%. However, the author also suggested that in the case of anticipated limitation in resources and time, the precision can be set at higher degree.

For current study, limitation in time and resources were expected, hence the d is set at 7.5% (d=0.075).

Thus, $n = (1.96/0.075)^2(0.37)(0.63) = 159$

For the second and third specific objectives, different method of sample size estimation was used (51), and the sample size estimated ranged from 67-107, depending on the number of significant associative independent variable that is expected out of current study.

With the inclusion of potential non-responders of 5%, the final sample size required was determined to be 167 subjects.

3.5 Sampling Method

Data collection process

The subjects undergoing MMT in the study location were approached when they attend the clinic for their daily dose of methadone or regular review. For subjects fulfilling inclusion criteria, complete patient information sheet were given to them for their reading before consent was acquired. Exclusion of subject was done according to exclusion criteria. Consented subjects

were then requested to complete a series of questionnaires, including a data form on socio-demographic and clinical characteristics, Brief Pain Inventory (BPI), Big Five Inventory (BFI), Beck's Depression Inventory (BDI), and Beck's Anxiety Inventory (BAI). The questionnaires were filled up there and then, after they have ingested their methadone of the day. For subjects who do not keen to participate, they will be assured that the standard of their MMT in the future will not be affected. This is explicitly stated in the patient information sheet to address issue of subjects' vulnerability.

Measuring instruments

Socio-demographic and clinical characteristic data form:

This questionnaire was self-generated by the author to gather information on age, race, gender, marital status, employment status and occupation, level of education ever attained, chronic medical illness, presence of mental illness, history of bone fracture, ongoing illicit substance use including kratom, current methadone dose, and any self-medication of pain by subjects, and duration of MMT since enrolment.

Brief Pain Inventory (BPI):

This is a widely used instrument in clinical pain assessment. It has been used in hundreds of studies, and has been shown to be an appropriated measure for pain due to wide range of clinical conditions (52). BPI was initially used to measure pain of malignancy, but it has been validated for use in study of chronic non-malignant pain as well (53). Tan and colleague demonstrated acceptable internal consistency of BPI, with Cronbach alpha coefficients of 0.85 for items of pain intensity, and 0.88 for items of pain interference. A validated Malay version of BPI is available for use, validated by Aisyaturridha and colleague (54).

The questionnaire measures pain at the 'sensory' dimension (pain intensity of severity) and the 'reactive' dimension of pain (interference with daily function).

Under the pain severity dimension, pain is assessed at its 'worst,' 'least,' 'average,' and 'now' (or current pain). For each of the above, subjects will be asked to score at a scale of 0 to 10, with '0' means 'no pain' and '10' means 'pain as bad as you can imagine' (52).

To measure how the pain has interfered with daily activities, the pain interference dimension is then used. For seven daily activities listed in the scale, the subjects will be asked to score at the scale of 0 to 10 on how much the pain had interfered with those activities, with '0' means 'does not interfere' and '10' means 'completely interferes'. Those activities are general activity, mood, walking ability, normal work (includes both work outside the home and housework), relationships with other people, sleep and enjoyment of life. Mean of the scores of seven interference items is used as the overall score, and this mean can be used if four out of the seven activities has been rated by a particular subject (52).

As an operational definition of chronic severe pain (CSP), current study will adopt the definition that has been used by previous studies (2, 4, 10), with some modification.

According to Rosenblum et al. and Barry et al., a subject is said to have CSP if he or she score 5 or higher on the BPI 'worst pain' scale in the past one week, or score 5 or higher on the BPI 'pain interference' scale. Pain duration should be more than 6 months. Karasz et al. used a wider definition, defining CSP as pain lasting longer than six months, with either pain severity or pain interference score of 5 or more, without specifying which subscale of pain severity or pain interference being referred to.

Referring back to the original author of BPI, Cleeland, in his manual he suggested researcher to use the mean of the seven interference score as the overall score of pain interference, and this mean can be use when at least four out of the seven interference item has been rated.

Thus for current study, the following definition of CSP was applied- A subject is said to have CSP if he or she score 5 or higher on the BPI 'worst pain' scale in the past one week, or obtain the mean 'pain interference' score of 5 or above, given that at least four out of the seven interference scales are scored. Furthermore the pattern of pain should present for at least 6 months.

Big Five Inventory (BFI):

BFI is a valid and reliable instrument to measure personality traits according to Big Five Theory or Five Factor Model of Personality (13, 55).

It is an efficient measuring instrument whereby it only takes about 5 minutes to be completed, as compared to NEO-FFI that usually take 15 minutes to complete. It was shown to be at least as efficient and easily understood as the 60 item NEO-FFI (55).

It has good internal consistency, as well as convergent validity with NEO-FFI (55).

The inventory consists of 44 items that measure Big Five attributes, ie Neuroticism (8 items), Extraversion (8 items), Agreeableness (9 items), Conscientiousness (9 items), and Openness (10 items). (56). However for current study, only the 8 Neuroticism items will be used to measure Neuroticism.

Validated Malay version of BFI was used for current study (57). The author of the validation study found that Confirmatory Factor Analysis (CFA) had shown sufficient evidence to demonstrate the conceptual equivalence between original BFI and Malay version of BFI. It was concluded that the results supported the fact that Western based Five Factor Model is valid cross-culturally in Eastern culture. Translated Malay version of BFI was shown to validly delineate personality within Malaysian context.

However, by using Hancock and Mueller's Coefficient H, the study demonstrated acceptable reliability (Coefficient H >0.70) for all BFI subscales except Openness to Experience. As the author proceeded to examine the validity of translated BFI scales, it was found that because of the low reliability of the Openness to Experience, the validity was acceptable only after excluding the scale from the original BFI. In other words, the modified translated BFI with only scales of Extraversion, Agreeableness, Concientiousness and Neuroticism showed acceptable validity (57).

BFI was chose instead of other available scale like NEO-FFI for current study despite the lack of extensive validation of the scale locally (in fact, the above mentioned study was the first conducted locally in translating and validating the scale). The use is justified by the fact that the scale is shorter, simpler and was shown to be easily understood by subjects answering the questionnaire. And because of financial resource limitation in current study, the fact that BFI could be used for free in research added more advantage to the use of the scale.

Beck's Depression Inventory (BDI):

BDI is a well-established self-reported instrument, and has been used by both Western and Eastern countries to measure depressive symptoms. It was first created by Aaron T. Beck and published more than 50 years ago (58). It has been translated into various languages, and its psychometric properties have been evaluated extensively (59, 60).

A few studies were carried out to examine the psychometric properties of BDI when being used in Malaysian population. Quek and colleagues has validated BDI in a study of patient with urological conditions, though in this study, majority of the subjects were Chinese (61). Mukhtar and Tian, in their study involving 1090 Malay subject form 4 distinct samples (students, general community, general medical patients, and patients with major depressive disorders), they concluded that Malay version of BDI is valid for use among Malay subjects in Malaysia, with good internal consistency (Cronbach's alpha ranging from 0.71 to 0.91), and good concurrent and discriminant validity (60)

Malay version of BDI, as the original version, consists of 21 items indicates various symptoms of depression. Subjects are evaluated on how they feel for the past one week. The first 13 items measure cognitive/affective component, whereas the subsequent 8 items measure somatic/performance component(60). Subjects are required to response to each item, indicating how severe the particular symptom is. Each item contains 4 responses with the score of 0 to 3. '0' indicates the absence of the symptom, whereas '3' indicates severe symptom.

Beck's Anxiety Inventory (BAI):

BAI is an instrument widely used for measurement of severity of anxiety symptoms, created by Aaron T. Beck and colleagues (62). It has been shown to have very good internal consistency, with Cronbach's alpha of 0.92, and high test-retest reliability (62). A Malay version of BAI is available and the psychometric properties of this has been examined preliminarily by Mukhtar and colleague, with Cronbach's alpha ranged from 0.66 to 0.89 and overall alpha value of 0.91, similar to other previous study done in Western and non-Western country. The concurrent validity of the instrument was found to be acceptable (63).

BAI consist of 21 questions about how a person feels for the past one week. Those 21 items are common symptoms of anxiety. The subject tested is required to choose, for each item, the severity of related symptom. Each item contains 4 responses with score ranged from 0 to 3, with '0' signify no such symptom at all and '3' indicate severe symptom.

CHAPTER 4: STATISTICAL ANALYSES

The data collected were analysed by using IBM SPSS Statistic version 22. The association between potential associative factors (numerical and categorical independent variables) and the presence of chronic severe pain (dependent variable) were first analysed by applying Simple Logistic Regression analysis (SLR). The associative factors with p value< 0.25 by SLR were then further analysed using Multiple Logistic Regression analysis (MLR). During the variable selection processes, forward selection was coupled with backward elimination in order to acquire preliminary main effect model. Alpha was set at 0.05. Multicollinearity and interaction were checked, and the fitness of the preliminary final model was assessed using Hosmer-Lemeshow test, classification table and area under the receiver operating characteristic (ROC) curve tests (64).

The main objective of the study was to look for association between neuroticism score and chronic severe pain, and other factors like BDI score, BAI score, daily methadone dosage and other characteristics were included as potential confounders to be controlled for. By using above statistical methods, this purpose could be achieved (64-66).

CHAPTER 5: MANUSCRIPT

5.1 Title page:

The Association between Chronic Severe Pain and Neuroticism Personality Trait among Patients on Methadone Maintenance Therapy in Alor Star, Kedah

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5.2 Abstract

The Association between Chronic Severe Pain and Neuroticism Personality Trait among Patients on Methadone Maintenance Therapy in Alor Star, Kedah

Introduction: Pain is very commonly reported among previous heroin users on methadone maintenance therapy (MMT) with the prevalence of chronic severe pain (CSP) of 37-48.2% being reported. The symptom causes distress and disability, and adversely affects patients' quality of life, addiction treatment outcome and exacerbates their ambivalence towards MMT. In general, neuroticism personality trait has been shown by various studies to be associated with CSP, but similar association has yet been explored in MMT patients.

Objectives: Current study aim to assess the prevalence of CSP among patients on MMT, and to examine whether neuroticism is significantly associated with CSP in this group of patients.

Method: This is a cross-sectional study, utilizing validated Malay versions of Brief Pain Inventory (BPI) for pain measurement, Big Five Inventory (BFI) to measure neuroticism, Beck's Depression Inventory (BDI) for measurement of depressive symptoms, and Beck's Anxiety Inventory (BAI) for measurement of anxiety symptoms. All rating instruments mentioned are self-rated instruments. Sample size is determined using proper sample size calculation, and universal sampling method is applied. Samples were collected from two MMT centres in Alor Star.

Results: Using Multiple Logistic Regression analyses, Neuroticism score ($p<0.001$), BAI score ($p=0.012$) and regular over-the-counter analgesic use ($p=0.016$) were found to be statistically significant in association with CSP, with adjusted Odds Ratio of 1.60 (95% CI 1.27, 2.12), 1.44 (95% CI 1.08, 1.93), and 3.56 (95% CI 1.27, 10.01), respectively.

Discussion: Neuroticism score is positively associated with CSP among patients on MMT, whereby with every one point increment in neuroticism score, there is 60% higher odds of having CSP. Other significant associative factors are BAI score and regular use of over-the-counter analgesics.

Keywords: *Neuroticism, chronic severe pain, methadone maintenance therapy (MMT)*

5.3 Introduction

Chronic severe pain among patients on methadone maintenance therapy and its implications

Pain is very commonly reported among previous heroin users on methadone maintenance therapy (MMT) with the prevalence of 37-61% (1-5). Chronic severe pain, on the other hand, was reported to have prevalence of 37-48.2% (2-4).These findings were rather high as compared to prevalence of 10% in general population (6).

Chronic severe pain (CSP) was reported to be highly problematic, with various implications. The implication of pain on people, specifically, patients on MMT is significant. Poorly controlled pain, especially chronic pain, has been shown to be associated with disability and distress (7), poor addiction outcome (2, 3), and poor quality of life among patients on MMT (8). Counselors also reported difficulties in helping patients on MMT with chronic pain (9). Chronic severe pain interfered with work and family life, obstructing the fulfillment of social obligation, and isolating patients from others. When undertreated, these symptoms can exacerbate patients' anxieties and ambivalence towards MMT (10).

Neuroticism personality trait and its clinical implications

Neuroticism is one of the personality trait in both the three and five factors models of personality, also widely known as the Big Three and Big Five theories, respectively (11). Traditionally, Eysenck referred to neuroticism as a trait of emotionality, specifically the tendency to arouse quickly when stimulated and to inhibit emotions slowly. Costa and McCrae defined neuroticism as a dimension of maladjustment or negative emotionality

versus adjustment and emotional stability (12). Others proposed that facets and correlated adjectives that describe neuroticism are Anxiety (tense), Angry hostility (irritable), Depression (not contented), Self-consciousness (shy), Impulsiveness (moody) and Vulnerability (not self-confident) (13). There were other slightly different definitions by other authors throughout the years, but the differences among definitions have been reconciled in the late 1990s with the consensus definition that, at its core, neuroticism is the propensity to experience negative emotions (12).

A person high on neuroticism is prone to experience chronic negative affect, psychological distress, and is at increased risk of developing psychopathology and mental illness (11, 12, 14-20).

Neuroticism is also being conceived as a vulnerability factor in pain perception. It lowers threshold at which pain is perceived as threatening, and at which pain catastrophizing emerges. Through structural equation modelling, a study had demonstrated that vigilance to pain is associated with heightened pain severity. Besides, it was found that pain catastrophizing and pain-related fear mediate the association between neuroticism and vigilance to pain (21).

When pain catastrophizing and pain coping strategies among subjects on MMT were being studied, it was found that subjects in group with CSP reported higher level of pain catastrophizing compared to subjects without CSP (22, 23). Addressing pain catastrophizing and pain concern among patient on MMT is crucial as this response to pain is associated with adverse pain-related clinical outcomes (23).

Overview of potential associative factors of chronic severe pain among patients on MMT

Chronic severe pain in this unique group of patients has been shown, by various studies, to be associated with myriad of factors.

Specific to patient on MMT, significant associations were found between CSP and mental illnesses like depression and anxiety disorders (1, 2, 4, 8, 24). Depression and anxiety disorders were found to be common among this group of patients (3, 5, 25-27).

Certain studies attempted to explore the association between CSP and daily dosage of methadone being prescribed to patient, and the results were rather inconclusive (3, 5, 28). Other studies advocated that long term use of opioids, like methadone, might actually cause opioid-induced hyperalgesia, where patient become more sensitive to pain perception as compared to unexposed individual (28-30).

On the other hand, it is well reported in various studies that kratom provide analgesic effect to people who use it regularly. It exerts its analgesic effect through activity on opioid receptors (31, 32). Kratom product was reported being used as opioid substitute by local people in countries of Southeast Asia like Thailand and Malaysia (31). However its chronic use leads to dependence and withdrawal, with symptoms similar to that of opioid use (33).

Pain symptoms has been shown to be associated with chronic medical illness (1-3, 5). Besides, chronic pain following orthopedic traumatic injuries and fractures were found to be common, although the injuries reported in these studies were heterogeneous in terms of nature and severity (34-36). Treating chronic pain due to traumatic injury with opioid analgesics had been shown to worsen pain symptoms and could lead to other psychopathologies (37).

It is a global phenomenon that, as a result of intravenous drug use, majority of active intravenous drug user (IVDU) or previous IVDU have hepatitis C viral infection, and many of them also have hepatitis B virus and HIV infection (38). These infections, especially hepatitis C virus and HIV has been suggested by some studies as a contributing factor in development of chronic pain (39-43), although another more recent study suggested otherwise (44).

From various evidences acquired so far, it is rather safe and reasonable to conclude that the determinants of chronic severe pain among MMT patients are likely to be complex.

Rationale of the study and research objectives

Methadone maintenance therapy is an important part of harm reduction program in Malaysia (45), and chronic severe pain has been show by various studies previously mentioned to be an important problem that might adversely affect its outcome.

Thus, current study aimed to determine the prevalence of chronic severe pain among patients on MMT in Alor Star, and further explores whether neuroticism personality trait is an associative factor of the distressing symptom. To the author's best knowledge, the postulated association has not yet been adequately and directly explored by other researcher. The author hoped that the findings of the study could help in improving the service of MMT in the future.

5.4 Methodology

Research design and data sampling

This is a cross sectional study, conducted in two centres for methadone maintenance therapy (MMT) in Alor Star. Data collection was done from July to September 2016. Inclusion and exclusion criteria were applied to screen for eligible subjects as they were being approached by researcher in respective methadone clinics.

For the purpose of determining prevalence of CSP in current study sample, the sample size was calculated using a formula to estimate a population proportion with good precision (46, 47).

$n= Z^2 [P(1-P)] /d^2$

P is the anticipated prevalence or population proportion. Estimated prevalence of CSP is taken as 37% (2, 4). Z value is set at conventional 1.96, for level of confidence of 95%. d is the absolute precision required to calculate sample size. According to Naing and colleagues, it is appropriate to have a precision of 5% (to be expressed as d=0.05) if the prevalence is expected to fall between 10%-90%. However, the author also suggested that in the case of anticipated limitation in resources and time, the precision can be set at higher degree. For current study, the precision was set at 7.5% (d=0.075).

For the objective of determining the association between neuroticism and CSP, different method of sample size estimation was used (48), and the sample size estimated ranged from 67-107, depending on the number of significant associative independent variable that is expected out of current study.

The two methods yield the sample size of 159. After included the non-responder rate of 5%, total subjects required was 167.

Total of 151 samples were successfully collected via universal sampling. It consisted of 104 subjects from Klinik Kesihatan Bandar Alor Star (KKBAS), and 47 subjects from Psychiatric Clinic of Hospital Sultanah Bahiyah. In the author's opinion, as the absolute precision of 7.5% and the power of 0.8 were being used for sample size calculation, with no non-responder, the number of sample collected is considered adequate.

Inclusion and exclusion criteria

Inclusion criteria were as follows.

- Individual age ranged from 18 to 65 years old.
- Subjects that have been in the therapy for at least 12 months, as pain should present for at least 6 months in order to be defined as chronic, and the subjects would require time to achieve stable dose of methadone.
- Subjects that consented for the study.

Subjects that were unable to complete rating instruments due to poor literacy and command in Malay Language were excluded from the study.

Recruitment of subjects

A complete patient information sheet was given to subjects that satisfied the inclusion and exclusion criteria for their reading, and the study was explained to them verbally, before consent being acquired. Consented subjects were requested to complete a series of questionnaires, including a data sheet on socio-demographic and clinical

characteristics, Brief Pain Inventory (BPI), Big Five Inventory (BFI), Beck's Depression Inventory (BDI), and Beck's Anxiety Inventory (BAI).

Patients who declined the invitation to participate were being assured that the standard of their MMT in the future will not be affected. This was explicitly stated in patient information sheet to address issue of subjects' vulnerability.

Rating instruments

Data sheets generated by the researcher were used to collect relevant socio-demographic and clinical data. Other rating instruments were further described below. The self-generated data sheets and all the following rating instruments were attached under the section of Appendix.

- **Brief Pain Inventory (BPI)**

This is a widely used instrument in clinical pain assessment. It has been used in hundreds of studies, and has been shown to be an appropriated measure for pain due to wide range of clinical conditions (49). BPI was initially used to measure pain of malignancy, but it has been validated for use in study of chronic non-malignant pain as well (50). Malay version of BPI was validated by Aisyaturridha and colleague (51)

- **Big Five Inventory (BFI) Neuroticism scale**

BFI is a valid and reliable instrument to measure personality traits according to Big Five Theory or Five Factor Model of Personality (13, 52). It is an efficient measuring instrument whereby it only takes about 5 minutes to be completed, as compared to NEO-FFI that usually take 15 minutes to complete. It was shown to be at least as efficient and easily understood as the 60 item NEO-FFI. It has good internal consistency, as well as