# PREVALENCE OF DERPESSION IN PATIENTS WITH DEMENTIA IN A TERTIARY GOVERNMENT HOSPITAL AND A TEACHING HOSPITAL IN KLANG VALLEY

**BY**

**DR LAYUZA BINTI ALIASAD**

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.....

Dr Zanariah Mat Saher

Consultant Psychiatrist and Psychogeriatrician

Department of Psychiatry and Mental Health

Kuala Lumpur Hospital.

**CERTIFICATION**

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.....

Dr Chong Lu-Ann

Psychiatrist and Lecturer

Department of Psychological Medicine

University Malaya.

**ABSTRACT**

**PREVALENCE OF DEPRESSION IN PATIENTS WITH DEMENTIA IN A TERTIARY HOSPITAL AND TEACHING HOSPITAL IN KLANG VALLEY**

***Introduction:*** Dementia is the most common illness that is associated with the geriatric age group. Depression occurs frequently in patients with dementia and has been well demonstrated to increased morbidity and mortality. However, there are limited data available in Malaysia pertaining to depression in patients with dementia.

***Objective:*** The main objective of this study is to determine the prevalence of depression in patients with dementia using GDS-15 and M.I.N.I and to examine the associated socio-demographic and clinical factors associated with depression among patients with dementia.

***Method:*** This is a cross sectional study on patients who have been diagnosed with dementia attending either psychogeriatric or memory clinic in HKL or memory clinic in UMMC. Their socio-demographic and clinical data were obtained by interviewing patients and care givers and also from the patients' records. The GDS-15 and M.I.N.I were used to determine the depression among subjects. Ethical approval to conduct this study was obtained from the UMMC ethics committee and from NIH through NMRR.

***Results:*** A total of 114 patients were recruited in the study. Prevalence of major depressive disorder based on GDS-15 score was 20.2% and prevalence of depression

using M.I.N.I was 10.5%. Depression based on GDS-15 was significantly associated with severity of dementia with adjusted odds ratio of 6 (p=0.006, CI=1.661-20.747). The MMSE score is negatively correlated with GDS-15 (r= -0.335, p<0.01).

***Conclusion:*** There was a high prevalence of depression in patients with dementia and it was significantly associated with the severity of dementia. Therefore, dementia patients should be regularly screened for depression during their clinic visit.

**ABSTRAK**

**PREVALENS KEMURUNGAN DALAM PESAKIT DEMENTIA DI HOSPITAL KERAJAAN TERTIARI DAN HOSPITAL PENGAJARAN DI LEMBAH KLANG.**

***Pengenalan:*** Dementia adalah penyakit yang paling kerap dikaitkan dengan golongan geriatrik. Kemurungan sering berlaku pada pesakit dengan dementia dan kemurungan menyebabkan peningkatan morbiditi dan mortaliti. Walau bagaimanapun, terdapat data yang terhad di Malaysia berkaitan dengan kemurungan pada pesakit dengan dementia.

***Objektif:*** Objektif utama kajian ini adalah untuk menentukan prevalens kemurungan pada pesakit dementia menggunakan GDS-15 dan MINI serta untuk mengkaji faktor sosio-demografi dan klinikal yang berhubungkait dengan kemurungan di kalangan pesakit dengan dementia.

***Kaedah:*** Ini adalah satu kajian keratan rentas pada pesakit yang telah didiagnosa dengan dementia yang menghadiri sama ada klinik psikogeriatrik atau klinik memori di HKL atau klinik memori di PPUM. Data sosio-demografi dan klinikal mereka diperolehi dengan menemuramah pesakit atau penjaga dan juga melalui rekod pesakit. GDS-15 dan MINI digunakan untuk menentukan kemurungan di kalangan subjek. Kelulusan etika untuk menjalankan kajian ini telah diperolehi dari jawatankuasa etika PPUM dan dari Institut Kebangsaan Kesihatan melalui NMRR.

***Keputusan:*** Sejumlah 114 pesakit telah menyertai kajian ini. Prevalens kemurungan dengan menggunakan GDS-15 skor adalah 20.2% dan prevalens kemurungan berdasarkan MINI adalah 10.5%. Kemurungan berdasarkan GDS-15 didapati berhubungkait dengan tahap penyakit dementia dengan pelarasan odds 6 (p=0.006, CI=1.661-20.747). Markah MMSE berhubungkait dengan GDS-15 secara negatif (r=-0.335, p <0.01).

***Kesimpulan:*** Terdapat prevalens kemurungan yang tinggi pada pesakit dengan dementia dan ia berhubungkait dengan tahap penyakit dementia. Oleh itu, pesakit dementia perlu mendapat saringan awal untuk mengenal pasti kemurungan semasa kehadiran mereka di klinik.

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## LIST OF ABBREVIATIONS

| | |
|---|---|
| AD | Alzheimer's Disease |
| BPSD | Behavioural and Psychological Symptoms of Dementia |
| CI | Confidence Interval |
| CRH | Corticotrophin-Releasing Hormone |
| DALYs | Disability Adjusted Life Years |
| DSM-IV-TR | Diagnostic Statistical Manual of Mental Disorder Edition IV Text Revision |
| GDS-15 | Geriatric Depression Scale 15 Items |
| HKL | Hospital Kuala Lumpur/Kuala Lumpur Hospital |
| HPA | Hypothalamic pituitary-adrenal |
| ICD 10 | International Classification of Diseases (Tenth Revision) |
| M.I.N.I | Mini International Neuropsychiatry Interview |
| MMSE | Mini Mental State Examination |
| NIH | National Institute of Health |
| NINCDS-ADRDA | National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorder Association |
| NINDS-AIREN | National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignment en Neurosciences |
| NMRR | National Medical Research Register |
| OR | Odds Ratio |
| PPUM | Pusat Perubatan Universiti Malaya |
| SD | Standard Deviation |

| | |
|---|---|
| UMMC | University Malaya Medical Centre |
| VaD | Vascular Dementia |
| WHO | World Health Organization |
| YLD | Year Lost to Disability |

# CHAPTER 1 INTRODUCTION

## 1. INTRODUCTION

The older or elderly person is defined as those who are 60 years old and above (World Health Organization [WHO], 2012). This is especially in the case in developing countries where the life expectancy levels are still low as compared to developed countries. The proportion of adult reaching old age has been increasing worldwide as a result of increase life expectancy (WHO, 2012) due to improvement in living conditions and advances in medical sciences.

Even though currently, Malaysia does not relatively have as high increase a number of proportions of ageing population compared to other developed countries, there is still an increase in absolute numbers of older persons in Malaysia compared to other age groups (Arokiasamy, 1999). For example, Malaysia also has rapid increase in proportion of the older people. The elderly population in Malaysia is expected to increase from 5.9% in 1991 to 9.9% by 2020 (Pala, 2005). The Population and Housing Census 2010 by Department of Statistics, Malaysia, also reported an increased in median age and the proportion of population aged 65 years and over which is parallel with the transition of age structure towards a rapidly aging population. The proportion of older person in Malaysia has been predicted to increase further to 20.8% by the year 2050 (Mujahid, 2006). In short, Malaysia faces many problem of a rapidly ageing population.

This trend of increase in the proportion of older population would pose multiple challenges for the health care providers, policy makers and government to improve and maintain good physical and mental health of the older persons. The main concerns of the increasing number of people reaching old age will be mainly reflected in burden of care in terms of social, economic and well-being of the older people (Chan, 2005).

The expected increase of disease burden as the number of people reaching old age is increasing. In 2002, the major contributors of the Year Lost to Disability (YLD) in Asia Pacific Region among all causes which include communicable, maternal, perinatal and nutritional conditions, non-communicable disease and injuries is neuropsychiatric conditions which is as high as 31.48% (WHO, 2002). The projected Disability Adjusted Life Years (DALYs) for persons aged 60 years and above in the year 2030 is expected to increase predominantly in the non-communicable diseases by 50%. This includes neoplasms or cancer, chronic diseases and neuropsychiatric conditions.

The most common neuropsychiatric condition associated with old age is dementia and disturbances of consciousness (Miyoshi & Morimura, 2010). Other neuropsychiatric conditions that are also associated in this age group include depression. The presentation of dementia, delirium and depression in elderly has overlapping symptoms that makes it a challenge to differentiate between these three conditions in this population of group. This issue is very pertinent and relevant in clinical settings in making the right diagnosis as these three conditions have different treatment pathways, both pharmacology and psychosocially. The relationships among these three disorders in the geriatric population had long been recognised as being bi-directional and complex (Ganguli, 2009)

Dementia is the most common illness that is associated with the older population group. The prevalence of dementia in low and middle-income countries of Western Pacific Region in the year 2004 was 5.1 million (WHO, 2004). The prevalence of dementia in Asia Pacific region was 13.7 million in 2005 and this figure is projected to increase to 84.6 million by 2050.

Whereas in Malaysia, 63 000 people are estimated to have dementia in 2005 with a projected increase of prevalence to 138 800 cases in 2050 (Alzheimer's disease International, 2006). The recent study by Hamid and colleagues found the prevalence rate of dementia was as high as 14.3%. Higher prevalence rate was found to be associated with older age, lack of formal education and Malay and Bumiputera ethnicity in this study (Hamid, Krishnaswamy, Abdullah & Momtaz, 2010).

It was highlighted that the main challenges in managing dementia in Malaysia are awareness and stigma (Nikmat, Hawthorne, & Ahmad Al-Mashoor, 2011). Malaysian like most Asian, do not perceived dementia as a disease but rather as part of normal aging. This lack of awareness leads to delay in the diagnosis and treatment (Tsolaki, Paraskevi, Degleris, & Karamavrou, 2009). The other challenges that Nikmat and colleagues brought up in their review were the availability of resources and support services to assist the elderly and the credibility of our health care professionals in terms of knowledge and expertise in providing the good level of health care to this group of older people (Nikmat *et al*., 2011).

The increased life expectancy is also translated indirectly into increased vulnerability to diseases and disabilities (Arokiasamy, 1999). Many studies showed that poor health and disabilities are associated with depression in elderly (Mohd Sidik, Rampal, Aini & Norhidayati, 2005; Djernes, 2006; Ma *et al*., 2008; Kua & Ho, 2008; Richardson *et al*., 2012).

It was estimated that the prevalence of unipolar depression in South East Asia was 40.9 million (WHO, 2004). Global Burden of Disease report by WHO 2004, revealed that the prevalence of depression in people aged 60 years and above in low-and middle-income countries of Western Pacific Region was 3.6 million. Unipolar depression makes a large contribution to the burden of disease, being at third place worldwide and eighth place in low-income countries. However unipolar depression was at the first place in middle- and high-income countries, in which Malaysia fall in to the category of middle-income country (WHO, 2004).

The prevalence of depression in Malaysia varies depending on the study populations. In a cross-sectional study done in primary care setting among adult patients, the prevalence of depressive disorder was 7.0% while prevalence of major depression was 5.6% (Jammy, Norlaili & Sherina, 2005). The prevalence of depression in the elderly will be discussed in the next chapter.

The association of depression and cognitive impairment or dementia is well established (Kennedy & Scalmati, 2001; Tekin & Cummings, 2001; Schweitzer, Tuckwell, O'Brien & Ames, 2002; Janzing, 2003; Modrego & Ferrandez, 2004; Djernes, 2006; Steffen &

Potter, 2008; Bangen *et al*., 2010; Li *et al*., 2011; Byers & Yaffe, 2012; Kessing VL, 2012; Barnes *et al*., 2012; Byers, Covinsky, Barnes & Yaffe 2012; Wang *et al*., 2012). The reported prevalence of depression in patients with dementia varies widely, most likely due to difference in methodology such as different type of dementia patients included in the study, measurement tools that were used and different setting of sample collection.

The prevalence of depression in patients with dementia ranges widely from 8% (Ballard, Bannister, Solis, Oyebode & Wilcock, 1996) to 86% (Bowirrat, Oscar-Berman & Logroscino, 2006) depending on the population of dementia patients that being studied and methodology differences in these different studies. There was a study that looking into the prevalence of depression in dementia sufferers in outpatient settings, which revealed 8% of the patient with dementia has depression (Ballard *et al*., 1996).

Depression is a source of excess morbidity and mortality in dementia patients (Lyketsos *et al*, 1997; Janzing, Bouwens, Teunisse, Van't Hof & Zitman, 1999; Suh, Kil Yeon, Shah & Lee, 2005; Porta-Etessam, Tobaruela-Gonzalez & Rabes-Berendes, 2011). Patient with dementia who has depression has a higher mortality rate compare to those without depression (Janzing *et al*., 1999; Suh *et al*., 2005). It was also found that the co-morbidity of depression in dementia patients would decrease the quality of life of the dementia sufferers (Lyketsos *et al.*, 1997). There is also increased need of institutionalization in dementia patients with depression (Kales, Chen, Blow, Welsh & Mellow, 2005; Pattanayak & Sagar, 2011).

There is also greater health care utilization in dementia patients with depression compare to those without depression (Kunik *et al*., 2003). Apart from that, co-morbid

depression in patients with dementia has been associated with decreasing caregiver's well being (Lyketsos *et al.*, 1997).

It is very important to detect depression in patient with dementia and to treat accordingly as it has been showed to be additional source of morbidity and mortality. To date, there is no local study carried out in Malaysia examining the prevalence of depression in patients with dementia. It is our hope that this study will provide more information regarding this important co-morbidity that carries such a high disease burden to both patients and care givers.

# CHAPTER 2 LITERATURE REVIEW

Literature review was carried out by searching Cohcrane Library, MEDLINE, PubMed, Wiley Online Library, Lippincott Williams and Wilkins Journals and other journal via Ovid, ProQuest or EBCOhost.

## 2.1 DEMENTIA

Dementia is one of the common neuropsychiatric conditions associated with old age. (Miyoshi & Morimura, 2010). According to the ICD-10 Classification of Mental and Behavioral Disorders, dementia is a syndrome due to disease of the brain, usually of a chronic or progressive nature, in which there is disturbance of multiple higher cortical functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgement. The conscious level is unclouded and the impairments of cognitive function are commonly accompanied, and occasionally preceded, by deterioration in emotional control, social behaviour, or motivation. (WHO, 1992).

In the Diagnostic Statistical Manual of Mental Disorder Edition IV Text Revision (DSM-IV-TR), dementia refers to a syndrome of acquired cognitive impairment, occurring in clear consciousness, sufficient to interfere with social and occupational functioning, and characterized by impairment in at least two cognitive domains (American Psychiatric Association, 2000).

The prevalence of dementia has been increasing due to the increasing lifespan of the older people. WHO reported that in 2004, prevalence of dementia worldwide was 24

million and according to World Alzheimer Report 2011, it was estimated 36 million people worldwide live with dementia in 2010 (WHO, 2004; Prince, Bryce & Ferri, 2011). This number is estimated to be double in 2030 and the increase is mainly in low- to middle-income countries (Prince *et al*., 2011). This is particularly challenging problem for Malaysia, which is a middle-income country, to have to face in the coming decades.

The prevalence of dementia in Malaysia from previous studies were varies on the measurement tools that being used, differences of demographic background and the study setting. The earliest study done by Krishnaswamy and colleagues and they found the prevalence of dementia in urban settlement to be 6% (Krishnaswamy, Kadir, Ali, Sidi & Matthews, 1997). Another study that was carried out in an elderly home care home reported that the prevalence of probable dementia was as high as 36.5% (Al-Jawad, Rashid & Narayan, 2007).

Norlaily and her team found that prevalence of dementia in the out-patient clinic of a teaching hospital in east coast of Peninsular Malaysia was much lower at 2.5% (Norlaily, Azidah, Asrenee, Rohayah & Juwita, 2009). In a nationwide study in 2005, the Mental Health and Quality of Life of Older Malaysian, prevalence rate of dementia was 14.3% (Hamid *et al*., 2010). The recent study in day care centres showed that 4% of the attendees had cognitive impairment (Sharifah Zainiyah *et al*., 2011).

Clinical features of dementia can be divided into cognitive and non-cognitive aspect. The cognitive symptoms include amnesia, apraxia, agnosia, aphasia and executive function (American Psychiatric Association, 2000). Symptoms of the non-cognitive aspect of dementia are functional decline and behavioural and psychological symptoms

of dementia (BPSD) that lead to increase in caregivers' burden. The Cache County study by Lyketsos and colleagues revealed that 60% of participants with Alzheimer's disease had one or more neuropsychiatric symptoms, of which 28% exhibited predominantly affective symptoms (Lyketsos *et al*., 2001)

There are many types of dementia but the common types of dementia are Alzheimer's disease, Vascular dementia, Mixed Alzheimer's disease and Vascular dementia, Dementia of Lewy Body, Fronto-temporal dementia and Parkinson's disease dementia. Other types of dementia include Human Immunodeficiency Virus complex and alcohol related dementia, demyelination, and Human Prion Disease including Creutzfeldt-Jacob dementia, Huntington's disease and Progressive Supranuclear Palsy. Alzheimer's disease is the most common type of dementia.

Alzheimer's disease is characterized by deficit in memory and one or more of language, praxis, recognizing and identify objects or executive functioning. The cognitive deficit is sufficient to cause impairment and decline in social and occupational functioning. The typical onset of Alzheimer's disease is gradual with insidious and progressive decline in cognitive function. All these symptoms must not be due to other central nervous system or substance-induced condition and must not exclusively occur during a course of delirium and not better accounted for by other psychiatric diagnosis (American Psychiatric Association, 2000). The certainty of the diagnosis of Alzheimer's disease was outline in the criteria developed by McKhann and team that 'definite Alzheimer's disease' confirm by brain biopsy or autopsy, 'probable Alzheimer's disease' has similar criteria as outline by American Psychiatric Association, 'possible Alzheimer's disease' has variation in the onset or course compare to typical Alzheimer's disease without a known aetiology and unlikely Alzheimer's

disease is when the patient presents a dementia syndrome with a sudden onset, focal neurologic signs, or seizure or gait disturbance early in the course of the illness (McKhann *et al*., 1984).

Pattern of symptoms of typical Alzheimer's disease patient usually started with transient changed in mood, followed by cognitive and functional decline in a linear pattern, subsequently neuropsychiatric symptoms and later progressive rigidity, akinesia and gait disability (Gauthier & Ballard, 2009)

Diagnostic criteria of vascular dementia includes decline in intellectual functioning sufficient to interfere with activities of daily life, not only due to the physical effect of stroke alone, evidenced by history, physical examination and/or neuroimaging examination of stroke; there must be also demonstrable temporal relationship between onset of dementia and stroke. The temporal relationship between the stroke and the dementia is manifested or inferred by the presence of one or more of onset of dementia symptoms within 3 months following a recognized stroke, such as abrupt deterioration in cognitive functions, or fluctuating, stepwise progression of cognitive deficits (Roman *et al*., 1994).

Fronto-temporal dementia is characterized by behavioural disturbances which includes disinhibition and early loss of personal and social awareness, affective symptoms such as emotional unconcern, anxiety or depression, speech disorder in which patient might present with progressive reduction of speech, stereotypies or perseveration and lastly physical signs such as primitive reflexes, incontinence, akinesia and rigidity (The Lund and Manchester group, 1994)

Dementia of Lewy Body is diagnosed when the patient presents with progressive cognitive decline that interfere with social and occupational functioning with symptoms such as fluctuating cognition with pronounced variations, recurrent visual hallucination or spontaneous motor features of parkinsonism. Diagnosis of possible Dementia of Lewy Body can be made if patients have one symptoms and probable Dementia of Lewy Body if patients have two symptoms (McKeith *et al*., 2005)

Parkinson's disease dementia is a dementia syndrome that may develop in the patients with already established Parkinson's disease with features of impairment in more than one cognitive domain, decline from pre-morbid level and the deficits must be severe enough to impair the daily life of the person independent of the impairment ascribable to motor or autonomic symptoms of Parkinson's Disease (Emre *et al*., 2007)

According to A Canadian Cohort Study of Cognitive Impairment and Related Dementias (ACCORD), the prevalence of Alzheimer's dementia accounted for 47.2% of the subjects, Mixed dementias was 33.7%, Vascular dementia was 8.7%, fronto-temporal degenerations was 5.4%, Dementia with Lewy bodies was 2.5%, while 1.8% were unclassifiable (Feldman *et al*., 2003).

A prospective naturalistic study by Lavretsky and colleague revealed that 53% of the participants diagnosed with Alzheimer's disease, Vascular dementia and Mixed Alzheimer's disease and Vascular dementia were 22% and 20% respectively (Lavretsky *et al*., 2010).

Whereas in a large community-based 15 years follow up study by Li and team reported that 58.7% of participant who developed dementia was diagnosed with Alzheimer's

disease, while 13.5% of them had vascular dementia, 17.2% with Mixed dementia and 10.6% were other forms of dementia (Li *et al*., 2011).

Severity of dementia can be divided into mild, moderate and severe. The severity of dementia is not based solely on the score of the measurement tool used to assess memory, but should include trained clinical assessment of the patient's level of cognitive functioning, activities of daily living and also communication. Patients with mild dementia who has difficulty in word finding during conversation and have mild difficulties in instrumental activities of daily living such as driving, shopping or finances may be able to live by themselves with minimal support. Those who have moderate dementia would have starting to have problem with basic activity of daily living such as dressing, grooming and bathing and using fragmented sentences, vague terms such as 'this' and 'that' to describe familiar everyday objects during conversations may not be able to live independently and need support from others. In severe dementia, speech would be so disrupted and they may be incoherent. Patients with severe dementia would have problems with all basic activities of daily living, including eating or walking (Vertesi *et al*., 2001)

## 2.2 LATE LIFE DEPRESSION AND COGNITIVE IMPAIRMENT

Depression is a major psychiatric illness which affected many people worldwide and results in significant morbidity and mortality. Depression would be define differently in different studies as the term depression includes minor depression, major depression, recurrent brief depression, dysthymic disorder, sub-syndromal or sub-threshold depression.

Based on Diagnostic Statistical Manual of Mental Disorder Edition IV Text Revision (DSM-IV-TR), clinical major depression is defined by the presence of one or two core symptoms; which are low mood and the inability to enjoy pleasurable activities most of the time for duration of at least two weeks. The core symptom must be accompanied by these associated symptoms, which are significant weight loss or weight gain or changes in appetite, insomnia or hypersomnia, fatigue, poor concentration or indecisive, psychomotor retardation or agitation, feeling of worthlessness or excessive or inappropriate guilt or recurrent thoughts of death or suicidal ideation or attempt; and total of five symptoms would fulfil the criteria of major depressive episode (American Psychiatric Association, 2000).

WHO reported that in the year 2004, unipolar depression is at third place worldwide, first place in middle to high income countries and eighth place in low-income countries in term of the burden of Disease. Malaysia which falls under the category of middle-income country, has a serious problem with depression in terms of burden of disease according to World Health Organisation (WHO, 2004). In the elderly population, defined as people aged 60 years and above, the prevalence of depression based on the Global Burden of Disease report by WHO 2004 in low-and middle-income countries of Western Pacific Region was reported as high as 3.6 million (WHO, 2004).

Life time prevalence on all categories under unipolar depression spectrum which include major depressive episode, minor depressive episode, recurrent brief depression and dysthymia was 20 to 25%. Major depressive episode is the most severe form of depressive disorder with the average life time prevalence was 12% (Sadock[1] & Sadock[2], 2007). From the gender perspective, women are more affected by depression. The Cache County study revealed that point prevalence of major depression in women and

men were 4.4% and 2.7% respectively while lifetime prevalence of major depression was 20.4% in women compare to only 9.6% in men (Steffens *et al*., 2000).

In a study of primary care attendees in Christchurch using the 15-item Geriatric Depression Scale (GDS-15) with cut-off of 5 and above, 10% of the elderly had significant depressive symptoms (Begg, Richardson & Wells, 2006). Whereas in our local setting, studies on the prevalence of depression in the elderly varies according to study design, scales that being used and the methodology, ranging from 5.6% to 25.3%. As mentioned earlier, the wide range of results varies according to study design, assessment tools used and population setting that were under study.

A local study of prevalence of depression in geriatric population among attendees of government primary clinic in Butterworth, Penang found that the prevalence of depression in those residing in rural area and urban area were 13.2% and 25.3% respectively (Mohd Sidik, Mohd Zulkefli & Shah 2003). Jammy and colleagues in their cross sectional study done in primary care setting among adult patients, revealed that prevalence of depressive disorder was 7.0% while prevalence of major depression was 5.6% (Jammy *et al.,* 2005). In a different study, set in an urban area in Selangor reported that prevalence of depression in elderly was 6.3% and cognitive impairment was found to be significantly associated with depression (Mohd Sidik *et al*., 2005).

There are some differences in symptoms of depression in elderly compare to adult. The depression in geriatric population is under recognized and undertreated due to the atypical presentation as the presence of co-morbid medical illness, cognitive impairment and adverse life events often complicates the diagnosis of depression (Sable, Dunn &

Zisook, 2002). A meta-analysis by Hegeman and colleagues highlighted that the phenomenology of major depression in older people are different compared with the younger people in term of more prominent presentation of agitation, general and gastrointestinal somatic symptoms including hypochondriasis, and less complaints of guilt and loss of sexual interest (Hegeman, Kok, Van Der Mast & Giltay, 2012).

Gallo and Rabins (1999) suggested that depressed elderly population might have alternative presentation of their depression such as unexplained somatic complaints, hopelessness, helplessness, anxiety and worries, memory complaints with or without objective sign of cognitive impairment, loss of feeling of pleasure, slowed movement, irritability, and lack of interest in personal care, such as poor adherence to medical or dietary regimens.

Kua and Ho (2008) in their review on subsyndromal depression in geriatric population suggested that poor health, brain injury, low folate and vitamin B12 and raised plasma homocysteine levels are risk factors for geriatric depression. A review by Djernes reported that the main predictors of depressive disorder and depressive symptoms cases in the elderly population are female gender, being single or divorced, living in the institutional care, chronic somatic illness, presence of cognitive impairment, functional impairment, lack of close social contact and prior history of depressive illness (Djernes, 2006).

In a study among older adult receiving Ageing Services Provider Network in Monroe County revealed that disability, number of medical conditions, number and severity of recent stressful events, low social support and low religiosity were independently associated with current major depression (Richardson *et al.*, 2012). According to a

large-scale survey on geriatric depression in Beijing, China, female gender, lower educational level, lower monthly income, rural abode and presence of one or more major medical conditions were associated with increased risk of geriatric depression (Ma *et al*., 2008).

While in our local study by Mohd Sidik and her colleagues, the associated factors for depression in elderly patients were female gender, unmarried patients, those without formal education, low total income and urban residence (Mohd Sidik *et al*., 2003).

As majority of older people would have co-morbid medical problem, they might be on several medications. These medications also might contribute to the depression. Anti hypertensive, digoxin, steroid and interferon are all known to be associated with depression (Sable *et al*., 2002).

The impact of depression in elderly is very serious. Generally, depression in elderly result in increase medical mortality and morbidity (Lavretsky *et al*., 2010), reduced quality of life (Blazer, 2003), functional and cognitive decline (Sable *et al*., 2002; Blazer, 2003; Modrego & Ferrandez, 2004; Steffens, 2009, Kommer *et al*., 2012) and increased medical care costs (Sable *et al*., 2002).

Byers and her team in their retrospective cohort study among older veterans reported that patients diagnosed with dysthymia or depression were twice likely to developed dementia compared with those without depression or dysthymia after adjusting for demographic and co-morbidities. They also found that the risk of death was more than 40% higher for those having depression or dysthymia compared with those who do not have depression or dysthymia (Byers *et al*., 2012).

According to Luber and colleagues in their study in the setting of primary care practice over 12 months revealed that depressed elderly patients had increased utilization of out-patients resources which include frequency of appointment, number of laboratory tests, x-rays and scans and consultations. This study also found that higher incidence of non specific medical complaints in depressed elderly patients compared with those without depression and these non specific medical complaints led to increased total ambulatory costs, test and consultations (Luber *et al*., 2001).

In a review by Butters and colleagues, the link between depression and dementia is clearly illustrated as in the figure below. Depression affects the hypothalamic pituitary-adrenal (HPA) axis in such a way that results in elevated corticotrophin-releasing hormone (CRH) with the nett effect of chronic elevation of adrenal glucocorticoid production which causes an impaired negative feedback loop and abnormal homeostatic regulation HPA. These disturbances causing prolonged hypercortisolemia that may lead to hippocampal atrophy and functional decline which further compromised the HPA regulation. All of these contributed to reduced brain or cognitive reserve that produces clinical manifestation of dementia. Therefore, according to Butter and her colleagues, depression is a risk factor for dementia especially in Alzheimer's disease (Butters *et al*., 2008)

Butters and colleagues also highlighted that association of late life depression with cerebrovascular changes that mediates the link between depression and dementia and this relationship between depression and vascular disease is bidirectional. Neurobilogically, depression worsened the outcome of vascular disease through systemic physiology derangement with hypercortisolaemia. In terms of lifestyle risks, individual with depression would also tend to neglect their health care apart from issue

of non adherence to treatment. This leads to increased risk of ischemia of the brain due to acute or chronic vascular disease. This further compromises and reduces the brain and cognitive reserved, resulting in the emergence of dementia symptoms. Cerebrovascular disease also caused ischemic changes in frontostriatal area that can cause depression that in line with vascular depression that coined by Alexopoulos (1999) and this would further lead to cascade of hypercortisolaemia and vascular events which, in vicious cycle, further leads to dementia (Alexopoulos, Bruce, Silbersweig, Kalayam & Stern, 1999; Butters *et al*., 2008). The figure below summarized and illustrates the proposed mechanism on depression increases the risk for Alzheimer's disease by Butters and colleagues (Butters *et al*., 2008).

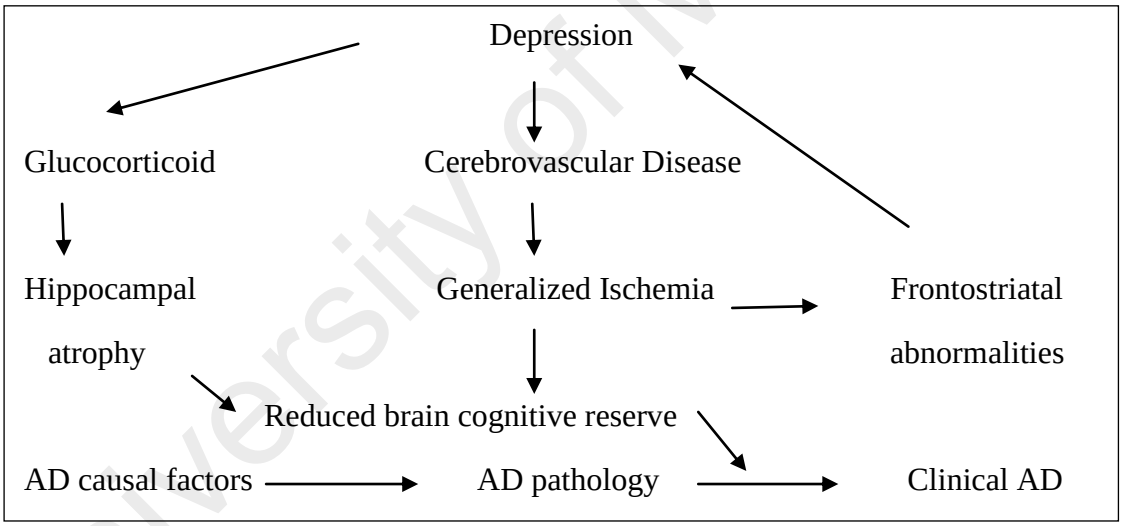


**Figure 2.1**: Proposed predominant mechanisms by which depression increases risk for Alzheimer's dementia (AD) *reproduced from Dialogues in Clinical Neuroscience 2008 with permission of the publisher (Les Laboratoires Servier, Suresnes, France).

The vascular burden in the link between depression in older people and dementia is also supported by another study that revealed that the severity of vascular burden was significantly correlated with depression severity and impairment of performance in

cognitive control and attention (Schneider, Ercoli, Siddarth & Lavretsky, 2012). The cognitive domains that were demonstrated to be associated in depression and dementia are cognitive control such as inhibition or mental flexibility, attention (Schneider *et al*., 2012), episodic memory (Barch *et al*., 2012) and executive function (Barch *et al*., 2012; Potter *et al*., 2012).

The advancement of imaging technique further demonstrates the link between depression and dementia better demonstrated. Steffens and colleagues found that small left hippocampal volume at baseline in older patients with depression were at higher risk of dementia later in life (Steffens *et al*., 2002). While Wang and his colleagues reported that those patients with late life depression and persistent cognitive impairment had decrease activation in the similar neural networks associated with the development of Alzheimer's disease and they suggested that measuring the neural activities in these regions might help to identify patient at risk of developing cognitive impairment (Wang *et al.*, 2012).

## 2.3 DEPRESSION IN PATIENTS WITH DEMENTIA

There are many studies to demonstrate the association between late life depression and dementia. Based on review by Tekin and Cummings, the relationship between depression and dementia is that depression can precede the dementia, and may be a risk factor for or co-exist as part of the presentation of dementia (Tekin & Cummings, 2001). It was found in many studies and reviews that late life depression is a prodromal phase of dementia, whereas recurrent depression might be etiologically associated with increased risk of dementia (Bassuk, Berkman & Wypij, 1998; Kennedy & Scalmati, 2001,; Li *et al*., 2011; Barnes *et al*., 2012; Kessing, 2012). However, there were also

studies that reported that only the most severe depressive cases and syndrome or persistent depressive episodes are the risk factors for dementia, and this association between depression and dementia does not apply to mild or episodic cases (Paterniti, Verdier-Taillefer, Dufouil & Alperovitch, 2002; Chen *et al*., 2008).

According to Jorm in his review, he highlighted that there was sufficient evidence that depression is possibly a risk factor for dementia and cognitive decline. He found that the depression was associated with an increased risk of subsequent dementia in both case-control studies with relative risk of 1.16-3.50 and also in prospective studies (Jorm, 2000). In another review, also by Jorm regarding the relationship between depression and dementia, he suggested that depression can be early prodromal phase of dementia, depression brings forward the clinical manifestation of dementia via damage of hippocampus through the glucocorticoid cascade (Jorm, 2001). Recent review by Enache, Winblad and Aarsland (2011) also supported that depression is a risk factor and prodromal phase for dementia of Alzheimer's type.

Depression is common and occurs frequently in patients with dementia (Janzing JGE, 2003). The prevalence of depression in patients with has a wide range from 8% in an out-patient memory clinic setting (Ballard *et al*., 1996) to 86% in a study of patients with Vascular dementia in an Arab community in rural Israel (Bowirrat *et al*., 2006). There were also a few studies looking into prevalence of depression in patients with dementia who residing in nursing home which found the prevalence rates to range from 19% (Payne *et al*., 2002; Verkaik, Francke, Meijel, Ribbe & Bensing, 2009) to 29% (Evers *et al*., 2002).

Depression was found to be more common in Vascular dementia compared with patients diagnosed to have Alzheimer's disease (Ballard *et al*., 1996; Bowirrat *et al*., 2006). This is not surprising according to the proposed mechanism between depression and dementia as proposed by Butters and colleagues (2008) illustrated earlier in Figure 2.1. According to a study by Bowirrat and colleagues, there is also an association between history of cardiovascular or cerebrovascular disease and depressive symptom in patient with Alzheimer's disease (Bowirrat *et al*., 2006). Bangen and her team reported that patients with Alzheimer's dementia with co-morbid depression demonstrated greater stroke risk burden relative to the cognitively normal group and those without depression (Bangen *et al*., 2010).

Barca, Engedal, Laks and Selbaek (2012) in their study showed that, a previous history of depression was significantly associated with development of depression in patient with Alzheimer's disease while the severity of dementia was associated with depression in group of patients with Fronto-temporal dementia, Vascular dementia, Dementia of Lewy Body or Parkinson's disease dementia.

Functionality of an elderly person is an important risk factor for depression in dementia patient. A study in a nursing home in Maryland revealed that, those patient with dementia that have co-morbidity of depression was significantly associated with more physical dependencies (Kaup *et al*., 2007)

The impact of depression in patients with dementia is very deleterious not only to the patients but also to the care givers. Depression has been well demonstrated to increased morbidity and mortality in patients with dementia (Lyketsos *et al*, 1997; Janzing *et al*., 1999; Suh *et al*., 2005; Porta-Etessam, 2011).

In term of impact of depression on the cognitive function itself, a longitudinal cohort study by Rapp and colleagues revealed that presence of depression in patient with dementia causes steeper cognitive decline (Potter & Steffens, 2007; Rapp *et al*., 2011). Presence of depression in patient with dementia produces significant functional impairment (Espiritu *et al*., 2001; Kales *et al*., 2005; Starkstein, Jorge, Mizrahi & Robinson, 2005; Potter & Steffens, 2007; Porta-Etessam *et al*., 2011); even in those patients with mild level of depression (Lyketsos *et al*., 1997; Starkstein *et al*., 2005).

In a prospective study by Kales and colleagues, patients with dementia who has coexisting depression utilises nursing home care services significantly higher compare to those who do not have this coexisting disorder (Kales et al., 2005). A study has shown greater health care utilisation in patients with dementia and co-morbid depression compare to those without depression (Kunik *et al*, 2003).

As the impact of depression in patient with dementia is detrimental, it is not surprising that the co-morbidity of depression in patients with dementia would significantly decrease the quality of life of the dementia sufferers (Lyketsos *et al*, 1997; Pattanayak & Sagar, 2011).

In addition to that, co-morbid depression in patients with dementia has been shown to be associated with decreasing caregiver's well being (Lyketsos *et al*, 1997). Last but not least, studies have also shown that patients with dementia who has depression has higher mortality rate compare to those without depression (Janzing *et al*., 1999; Suh *et al*., 2005).

# CHAPTER 3 RATIONALE AND OBJECTIVES

## 3.1 Rationale of study

There were quite numbers of studies about the depression in patients with dementia worldwide, however, there was no such study done locally based on the literature review. This study will look into the prevalence of depression in dementia patients in the local setting using a specific questionnaire. This is study is important to increase the awareness and highlight about the depression in patients with dementia in our local setting. As depression may be influenced by social values, a local data is more relevant for health care provider in planning intervention program for the target group of elderly people with dementia in our country.

It is important to have our own study about the depression in patients with dementia as it is clear demonstrated above in my literature review that the adverse effects of untreated depression both in the aetiology and prognosis of dementia. It is also paramount to raise awareness and highlight the debilitating effect of depression in patients with dementia in our local setting. Data on prevalence of depression in patients with dementia collected in a local setting is more relevant to convince local healthcare providers to plan and allocate resources to help health professionals provide treatment and support both for the patients with dementia and co-morbid depression in our country.

The screening and detection of depression and antidepressant treatments are more cost effective than the measures that need to be done to management the impact of the

depression in dementia. In the long run, early detection and treatment for depression in patients with dementia will have a huge impact on health care utilisation and later institutionalisation. The first step towards this goal is to examine the prevalence of depression in patients with dementia in our local setting, which has not been studied before in our local setting.

### 3.2 General objectives

The general objective of this study is to determine the prevalence of depression among patients with dementia attending outpatient psychogeriatric or memory clinic in Hospital Kuala Lumpur and memory clinic in University Malaya Medical Centre.

### 3.3 Specific objectives

1. To determine the prevalence of depression among patients with dementia using the Geriatric Depression Scale 15 items (GDS-15) either using English version or Malay version.

2. To determine the prevalence of depression among patients with dementia using Mini International Neuropsychiatric Interview (M.I.N.I.).

3. To describe the association between patients with dementia who are depressed with the socio-demographic and clinical factors.

### 3.4 Research hypothesis

1. There is a significant prevalence of depression in patients with dementia.

2. There is significant association between socio-demographic (gender, marital status, educational level, family income, living status) and clinical factors (type of dementia, severity of dementia, duration of diagnosis and antidementia medication) of patients with depression in dementia patients.

# CHAPTER 4 METHODOLOGY

## 4.1 Study setting

This study involved two large hospitals which are Kuala Lumpur Hospital (HKL) and University Malaya Medical Centre (UMMC). Both of these hospitals are located in the Klang Valley area.

Kuala Lumpur Hospital is a tertiary government hospital under the Ministry of Health Malaysia. It is the largest hospital under the Ministry of Health. Kuala Lumpur Hospital has 49 departments and units; which include 27 clinical departments and 12 clinical support services, administration, finance, pharmaceutical, training and research department.

The Department of Psychiatry and Mental Health is situated in Institut Kajisaraf Tunku Abdul Rahman building. The department offers outpatient clinic, inpatient services and community psychiatry services. The Psychogeraitric clinic is held on every Tuesday and Wednesday morning in the Psychiatry Clinic and runs by a psychogeriatric consultant, a specialist and medical officer. There are about average 20 patients in each clinic sessions.

The Memory clinic is held on Thursday afternoon in the Physician clinic at the first floor of main building and it is under the Geriatric Unit of Medical Department. The Memory clinic is jointly run by the Medical Department and the Psychiatry and Mental Health Department. The patients who attend the Memory clinic will be seen by Consultant geriatricians, Physicians or Psychogeriatrician. The clinic provides medical

services for up to 30 patients per clinic session. The patients were referred from other department within the HKL or from other hospitals, institutions or agencies.

University Malaya Medical Centre is under the Ministry of Higher Education. It is the first teaching hospital in Malaysia. University Malaya Medical Centre is situated at the border of Kuala Lumpur and in the city of Petaling Jaya. UMMC provides medical services for patients from Kuala Lumpur and Selangor, mainly from Petaling Jaya. The population that covered by UMMC is about 610 000 people. The majority of the population are Chinese and Malays, and followed by Indians and other races (Department of Statistics, Malaysia, 2010).

The Memory Clinic in UMMC is also jointly run by the Medical Department and the Department of Psychological Medicine. It is held on every Thursday afternoon and it provides medical services for up to 30 to 40 patients each clinic session.

**4.2 Study Design**

This is cross sectional study involving dementia patients who attend psychogeraitric clinic and memory clinic in Kuala Lumpur Hospital and memory clinic in University Malaya Medical Centre.

**4.3 Period of Study**

This study was conducted from September 2012 until mid January 2013 for a period of five months.

### 4.4 Study Population

The study population were all patients attending psychogeraitric clinic and memory clinic in Kuala Lumpur Hospital and memory clinic in University Malaya Medical Centre.

### 4.5 Sampling Method

This study was conducted using the convenient sampling method. All patients who were diagnosed to have dementia attending psychogeriatric clinic or memory clinic in Hospital Kuala Lumpur and memory clinic in University Malaya Medical Centre during the study period, who fulfilled the inclusion criteria and consent to participate in study obtained from either patients or caregiver when approached by the researcher are recruited into the study.

### 4.6 Inclusion criteria

1. Age 60 and above.
2. Patients with mild to moderate dementia (MMSE score of 10 or more).
3. Patients stay with family or has caregiver from nursing home as collection of sociodemographic data would need collateral input from family or caregivers.
4. Patients, family or caregiver understand English or Malay and are able to understand the questionnaires.
5. Patients or caregiver consented to the study.

### 4.7 Exclusion criteria

1. Patients who could not understand or communicate in Malay or English.
2. Patients with MMSE score of less than 10.

### 4.8 Study Variables

1. All the demographic data such as age, marital status, level of education, history of employment, children and household income were obtained from the caregiver and/or patient.
2. The type of dementia diagnosis by the treating psychiatrist or physician, the duration of the illness, necessary screening investigations including blood investigation and the brain imaging result were made available to the researcher.
3. Background medical co-morbidity, previous psychiatry history and patient's current medications were made known to the researcher from the patient's record or case notes.
4. The Mini Mental State Examination (MMSE) and Mini International Neuropsychiatric Interview (M.I.N.I) were assessed by the researcher.
5. The Geriatric Depression Scale-15 (GDS-15) was carried out by the patients themselves except for small numbers of patients who cannot read. The researcher will help to read out the Geriatric Depression Scale-15 for the patients who cannot read.

## 4.9 Operational Definition

1. Medical problem – any patients who were diagnosed and/or treated for having medical illnesses such as diabetes mellitus, hypertension, hypercholesterolaemia, ischemic heart disease, Parkinson's disease and other medical illnesses.

2. Past psychiatry history – any patient who reported ever been diagnosed and/or treated for psychiatric illness in the past such as bipolar disorder, depressive disorder, schizophrenia and other psychiatric illnesses and the diagnosis confirm from patient's record based on DSM IV-TR criteria.

3. Duration of diagnosis – based on how many years from patient first diagnosed with dementia in psychogeriatric or memory to the reference year of study period which is 2012.

4. Types of dementia – diagnosis and type of dementia were diagnosed by expert and trained consultant geriatrician or psychogeriatrician based on criteria from DSM IV-TR or ICD 10 diagnoses supported by the result of investigations.

5. Depression – probable depression is based on the Geriatric Depression Scale-15 score of 5 or more. Depression with GDS-15 cut off 5 or more will include minor or mild depression and major depression.

6. Major depressive disorder – diagnosis of depression based on presence of depressive symptoms that fulfilled the criteria to diagnosed major depressive episode in M.I.N.I module A that include lifetime and current diagnosis.

### 4.10 Data collection

Pre test was done on 30 August 2012. The sets of questionnaires were tested on 5 patients who attend psychogeriatric clinic. The purpose of this pre test is to identify any possible problem or difficulty that could arise in order to complete the sets of questionnaires. The pre tests were also done to estimate the time that needed to complete all the questionnaires by the patients during the clinic session and to see which time is better for the patient to answer the questionnaires, either before or after they see the doctor. During the pre test, researcher found out that it was more feasible to get the patients to answer the questionnaires while waiting for their turn to see the doctor.

During the recruitment session, the patients with dementia who attended the psychogeriatric or memory clinic for follow up were indentified at the counter when they registered their attendance. Their case notes were assessed and those eligible for the study were approach to participate in the study. The patients and the caregivers were then given the Patients Information Sheet and briefed about the study. If the patients and caregivers understand the purpose of the study and agree to participate in the study, the informed consent would be obtained and they would be recruited in this study.

Socio-demographic data were firstly collected from patients and the caregivers followed by the MMSE. Then, the patient will answer the Geriatric Depression Scale by themselves except for small numbers of patients who cannot read that the researcher will help to read out the GDS-15. After that, the patients were interviewed by the researcher using a diagnostic scale (MINI) to confirm the diagnosis of major depressive episode.

Finally, the researcher would complete the data collection by obtaining the clinical variables from the patient's case notes or records. Total duration of assessment and interview takes around 30 to 45 minutes for each patient.

### 4.11 Sample size

The sample size was calculated using the formula of sample size calculator for prevalence study (Naing, Winn & Rusli, 2006)

$$N = \frac{Z^2P(1-P)}{d^2}$$

N – sample size

Z – Z statistic for level of confidence

P – expected prevalence

d – Precision

There is no available local prevalence of depression in patients with dementia. In the current study, the prevalence rate was taken as 8% based on the similar study by Ballard et al. (1996) looking at the prevalence rate of depression in dementia sufferers from the outpatient setting.

Z value for the level of confidence of 95% is 1.96. The precision, d was set at 5%. The sample size calculated as below:

$$N = \frac{1.96^2(0.08)(0.92)}{0.05^2} = 114$$

For this study, the sample size that will be targeted for is 114 patients.

### 4.12 Study Instruments

#### 4.12.1 Socio-demographic and clinical profile questionnaires

A set of questionnaire was developed by the researcher to collect the relevant social demographic and clinical profile from the participating subjects.

The first part of the questionnaires consisted of questions on socio-demographic data which included the subject's age, gender, marital status, level of education, history of employment and number of children.

The second part of the questionnaires consisted of the questions on the clinical profile that would gather data on the type of dementia, the duration of illness, medications that patients are currently on and support from non-government organization.

#### 4.12.2 Mini Mental State Examination (MMSE)

The Mini Mental State Examination (MMSE) is widely used to screen for cognitive impairment in person suspected to have dementia and it is a valid and reliable tool. MMSE was devised by Folstein et al. that consist of 11 questions and only takes about 10 minutes to be administered to the adult and elderly (Folstein[1], Folstein[2] & McHugh, 1975). It is a quantitative measure of cognitive status hence can be used to screen for cognitive impairment, to estimate the severity of cognitive impairment at the time of assessment, to follow the changes of cognitive impairment over time and also to document the patient's response to treatment.

The MMSE has total score of 30 points and it has 5 domains which assess orientation, registration, attention and calculation, recall, language and praxis. The score of MMSE are categorized as mild with score 20 or more, moderate with score of 10 till 19 and severe with score less than 10 (Forchetti, 2007). Those patients with MMSE less than 10 which fall under the category of severe dementia would be excluded from this study as they might have issues in understanding and answer the questionnaires.

In this study, we use English and Malay version of MMSE; with the Chinese subjects would also be given the template of Chinese version of MMSE on the domain of language only if they have difficulty writing or reading either in English or Malay. As we are using serial-7 test instead of using the other option of serial 3 or speliing 'Dunia' backwards, we choose Malay version of MMSE that was validated by Zarina and colleagues. This first validation of Malay version of MMSE were done in subjects who stay in old folks home located in Kelantan, Perak, Kuala Lumpur and Penang which are among the 4 states in Peninsular Malaysia

This Malay version of MMSE by Zarina and colleagues (2007) revealed suggest different cut off points depends on the subjects' level of education. For the illiterate subjects, cut off score 14 had sensitivity and specificity of 35.4% and 76.8% respectively. The MMSE cut off score 17 was suggested for patients who completed primary education with sensitivity of 56.6% and specificity of 93.8%. For subject with secondary education, the cut off score of 22 had higher sensitivity of 92% and specificity of 92.2% compared to other level of education.

In our study, we are using the MMSE score to group the patients according to the severity of dementia either mild or moderate based on the MMSE score (MMSE score

of 20 or more as mild, MMSE score of 10 till 19 as moderate). We did not specify any cut off score of MMSE for diagnosis of dementia as all the subjects must be diagnosed as dementias first before entering this study.

### 4.12.3 Geriatric Depression Scale 15 items (GDS-15)

The Geriatric Depression Scale (GDS) is a self rating scale devised to screen for depression in the population of elderly. The original version of GDS consisted of 30 questions with yes or no answer in reference on how they felt the past week (Yesavage *et al*., 1983).

The shorter version of GDS was developed in 1986; consisted of 15 questions (GDS-15) that was selected from the original version of GDS that had highest correlation to depressive symptoms in the validation studies (Sheikh &Yesavage, 1986). The GDS-15 is easily used by the physically ill and mild to moderate dementia that has short attention span and easily feel fatigue. Systematic review by Wancata and colleagues revealed that both GDS-30 and GDS-15 had similar validity indices (Wancata, Alexandrowicz, Marquat, Weiss & Friedrich, 2006). Study on residents in a nursing home also concluded that there was no difference of the two versions of the GDS in sensitivity and yielded potential added value in medical settings (Mitchell, Bird, Rizzo & Meader, 2010)

Study by Snow and colleagues (2005) showed that the diagnosis of dementia per se did not predict inaccuracy in self report depression in patients with dementia (Snow *et al*., 2005). The Geriatric Depression Scale is a valid and reliable measure for depression in patients with dementia especially in mild to moderate dementia as revealed by studies

done in population of elderly with dementia in different settings (Feher, Larrabee & Crook, 1992; Ward, Wadsworth & Peterson, 1994; Lach, Chang & Edwards, 2010; Lopez, Quan & Carvajal, 2010).

For this study, we had used cut-off point of 5 and above for caseness (depression) as suggested by many studies that revealed optimum sensitivity and specificity in geriatric population (Lyness *et al*., 1997; Almeida[1] & Almeida[2], 1999; Marc, Raue & Bruce, 2008; Steffens, 2009) and also in studies done on patients with dementia (Muller-Thomsen, Arlt, Mann, Mab & Ganzer, 2005; Korner *et al*., 2006; Lach *et al*., 2010). The sensitivity and sensitivity of GDS-15 with cut-off point 5 and above in these studies on patients with dementia were ranging from 84.2% to 87% and 68.8% to 83% respectively (Korner *et al*, 2006; Lach *et al*., 2010).

This scale has been translated and validated into different languages. The Malay version of GDS was validated by Teh and Hasanah (2004) with satisfactory reliability (Cronbach's alpha = 0.84, test-retest reliability = 0.84) and concurrent validity with Montgomery –Asberg Depression Rating Scale (MADRS) by Spearman's rho was 0.68. This validation study was done in physically ill elderly inpatients who were admitted in either medical, surgical or orthopaedic wards in a teaching hospital in East coast of Peninsular Malaysia. The study also found out that the Item 9 from the Malay version of GDS could not differentiate between cases and non-cases. The cut-off point 5/6 of Malay version of GDS-14 was 95.5% sensitive and 84.2% specific in detecting all clinically significant depression. However, to date, no study was done to validate the Malay GDS in patients with dementia as this study exclude patients with significant cognitive impairment.

As we use both English and Malay version of GDS in this study; we would use Malay GDS 15 instead of 14 items for more standardized scoring and comparable data with the English version.

### 4.12.4 Mini International Neuropsychiatric Interview (M.I.N.I) Version 6.0.0

Mini International Neuropsychiatric Interview (M.I.N.I) is a short structured diagnostic interview design to diagnose the DSM-IV and ICD 10 psychiatric disorder. It is relatively brief instrument that is divided into modules which is corresponding to diagnostic categories such as major depressive episode, dysthymia, mania/hypomania, panic disorder, social phobia, post traumatic stress disorder, psychotic disorders, non alcohol psychoactive substance use disorders, anorexia nervosa and generalized anxiety disorder (Sheehan *et al*., 1998). The MINI has a good validity and reliability. It is a short but accurate structured interview and has been used in many clinical trials and epidemiological studies. According to study done by Pinniti and team (2003), they found out that MINI can be easily used in routine clinical interviews and had a good acceptance by patients (Pinninti, Madison, Musser & Rissmiller, 2003).

MINI has been used in studies on elderly population to diagnose depression in elderly (Ritchie *et al*., 2004; van't Veer-Tazelaar *et al*., 2009). MINI was proved to be able to diagnose depression in Alzheimer's disease (Engedal, Barca, Laks, Selbaek, 2011; Starkstein, Dragovic, Jorge, Brockman & Robinson, 2011; Brockman, Jayawardena & Starkstein, 2011) even though there was modified version of DSM-IV criteria by the National Institute of Mental Health provisional diagnostic criteria for depression in Alzheimer's Disease (NIMH-dAD). Engedal and colleagues (2011) and Starkstein and

team (2011) suggested that DSM-IV criteria for major depression is sufficient enough without any modification to diagnose depression in dementia patient. They did studies to compare with the National Institute of Mental Health provisional diagnostic criteria for depression in Alzheimer's Disease (NIMH-dAD) to detect depression in patients with dementia and it showed no significant different when using both criteria.

In this study, the patients were interviewed based on MINI to confirm the diagnosis of major depressive disorder after they completed the GDS. In terms of past episode, the caregivers input would also obtain as patient might have problem with remote memory.

Researcher has been using all the study instruments above in daily clinical practice.

### 4.13 Flow Chart of Patients' Recruitment

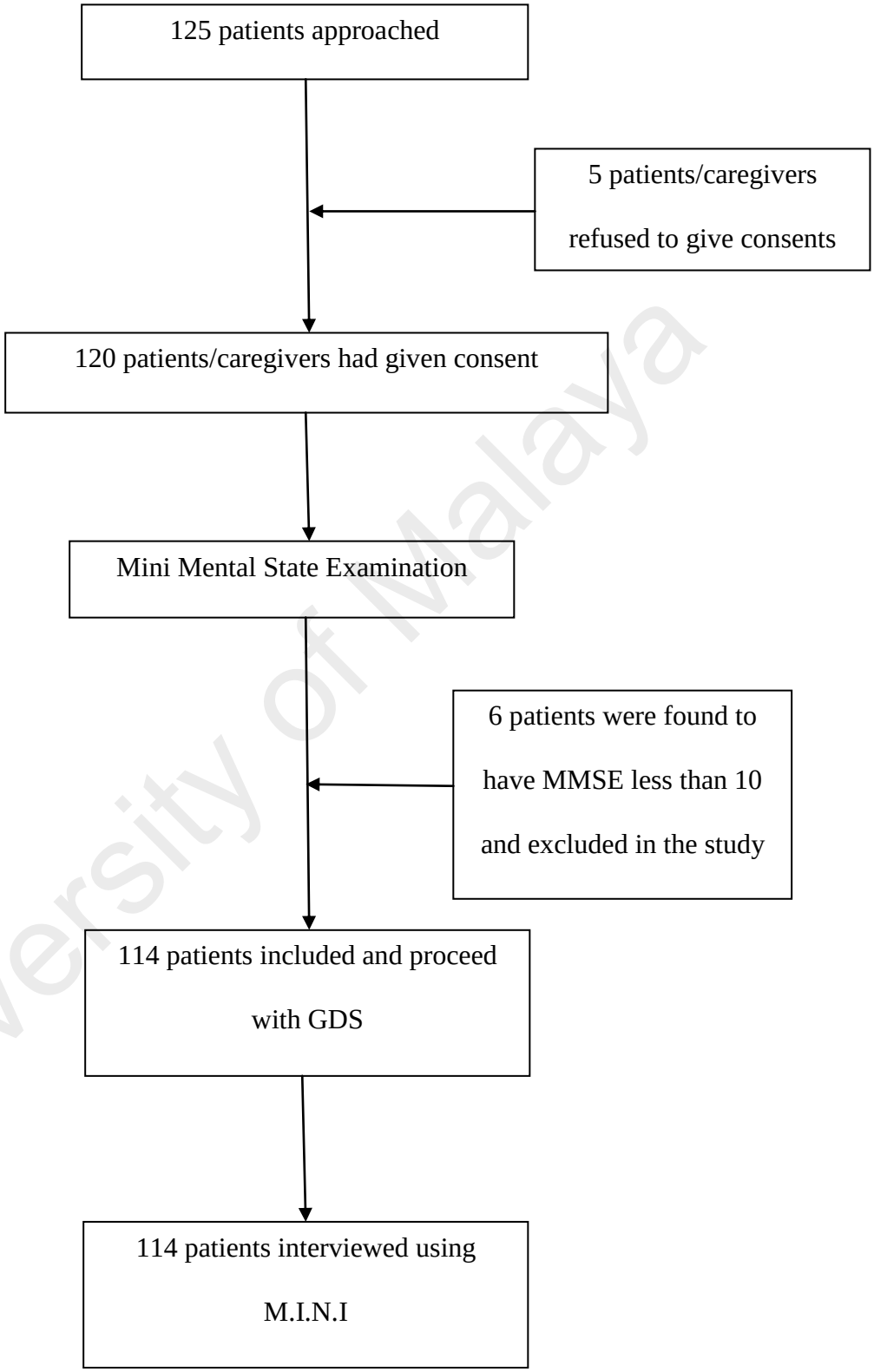


**Figure 4.1** Algorithm of patients' recruitment and data collection

### 4.14 Statistical Analysis

The data was analyzed using the Statistical Package for Social Sciences (SPSS) Version 20. Prevalence of major depressive disorder based on MINI and possible cases of depression based on GDS score with respective cut-off point were determined.

The summaries of socio-demographic and clinical variable were done using the descriptive statistic. The relationships of GDS-15 score as dependent continuous variable and the socio-demographic and clinical variables as independent variable were analyzed using the Mann U Whitney test as Kolmogorov-Smirnov test showed that the GDS score was not normally distributed. The correlation between the GDS score and the MMSE score would be analyzed using Spearman correlation.

The relationship between the Major depressive disorder based on MINI and the socio-demographic and clinical variables were analyzed using Chi square test.

Later, regression analyses were carried out to study the strength of association between the outcome and factors of interest with adjustment for covariates/confounders.

We had also look into the relationship between GDS (patients who had scored 1 in each item of GDS) with the severity of dementia based on the score of MMSE using Chi square test.

### 4.15 Ethical Consideration

This study was approved by the Research Committee, Department of Psychological Medicine in December 2011 and by Research and Ethics Committee, University Malaya Medical Centre in 15 August 2012 (Reference number: 938.12).

The National Institute of Health through National Medical Research Register has given approval on 29 August 2012 for this study to be conducted in Kuala Lumpur Hospital (Reference number: NMRR-12-576-12529).

The informed consent was obtained from either the patient or the caregiver. All patients were reassured of the confidentiality of the information given during the study.

# CHAPTER 5 RESULTS

## 5. RESULTS

During the study period of 5 months, a total of 125 patients attended psychogeriatric or memory clinic in UMMC and HKL were approached to participate in this study. However, 4 patients or care givers refused to give consent as they could not speak and read in Malay or English and 1 patient refused to give consent due to time constraint. Subsequently, another 6 patients were excluded in the study as the Mini Mental State Examination score was less than 10. In the end, only a total of 114 patients were recruited in this study. Majority of the patient were from University Malaya Medical Centre with 73 patients (64%) while 41 patients (36%) were from Hospital Kuala Lumpur.

### 5.1 Socio-demographic profiles of the study samples

The mean age group for the sample in this study was 76.1 years with standard deviation of 7.1 years (Figure 5.1). More than half of the samples were female (59.6%) whereas male samples were 46% (Figure 5.2). Majority of the patients were Chinese that comprised of 69 patients (60.5%) followed by 23 Malay samples (20.2%), 19 Indian samples (16.7%) and 3 others (2.6%). 60.5% of samples were married, while 32.5% were widowed, 6.1% were single and only 1 person was a divorcee (0.9%). (Table 5.1)

Majority of the patients have children (93%). Only 1 patient was still working (0.9%) while majority of them were retired (78.9%) and 20.2% of samples were housewife (Table 5.1). 90.4% of samples were staying with the family members while the remaining 9.6% were staying in nursing home (Figure 5.3).

Ten patients (8.8%) did not have any formal education while 45 patients (39.5%) had at least primary level of education, 43 patients (37.7%) had at least secondary level of education and 16 patients (14%) had tertiary education (Figure 5.4).

More than half of the samples (66.7%) were found to have family income of more than RM 2000 per months, followed by 23.7% of samples who had family income of RM 1000 to RM 2000 per month and 9.6% of samples had family income of less than RM 1000 per month (Figure 5.5)

**Table 5.1** Descriptive characteristic of socio-demographic data (N=114)

| Socio-demographic profile | N (%) | Mean(SD) |
|---|---|---|
| **Age** | | 76.1 (7.1) |
| **Centre** | | |
| Kuala Lumpur Hospital | 41 (36.0) | |
| University Malaya Medical Centre | 73 (64.0) | |
| **Gender** | | |
| Male | 46 (40.4) | |
| Female | 68 (59.6) | |
| **Race** | | |
| Malay | 23 (20.2) | |
| Chinese | 69 (60.5) | |
| Indian | 19 (16.7) | |
| Others | 3 (2.6) | |
| **Marital status** | | |
| Married | 69 (60.5) | |
| Widowed | 37 (32.5) | |
| Divorced | 1 (0.9) | |
| Single | 7 (6.1) | |
| **Children** | | |
| Yes | 106 (93.0) | |
| No | 8 (7.0) | |
| **Employment status** | | |
| Employed | 1 (0.9) | |
| Retired | 90 (78.9) | |
| Housewife | 23 (20.2) | |
| **Living status** | | |
| Living with family | 103 (90.4) | |
| Living in nursing home | 11 (9.6) | |
| **Educational level** | | |
| No formal education | 10 (8.8) | |
| Primary education | 45 (39.5) | |
| Secondary education | 43 (37.7) | |
| Tertiary education | 16 ( 14.0) | |
| **Family income** | | |
| Less than RM 1000 | 11 (9.6) | |
| RM 1000 – RM 2000 | 27 (23.7) | |
| More than RM 2000 | 76 (66.7) | |

SD=standard deviation

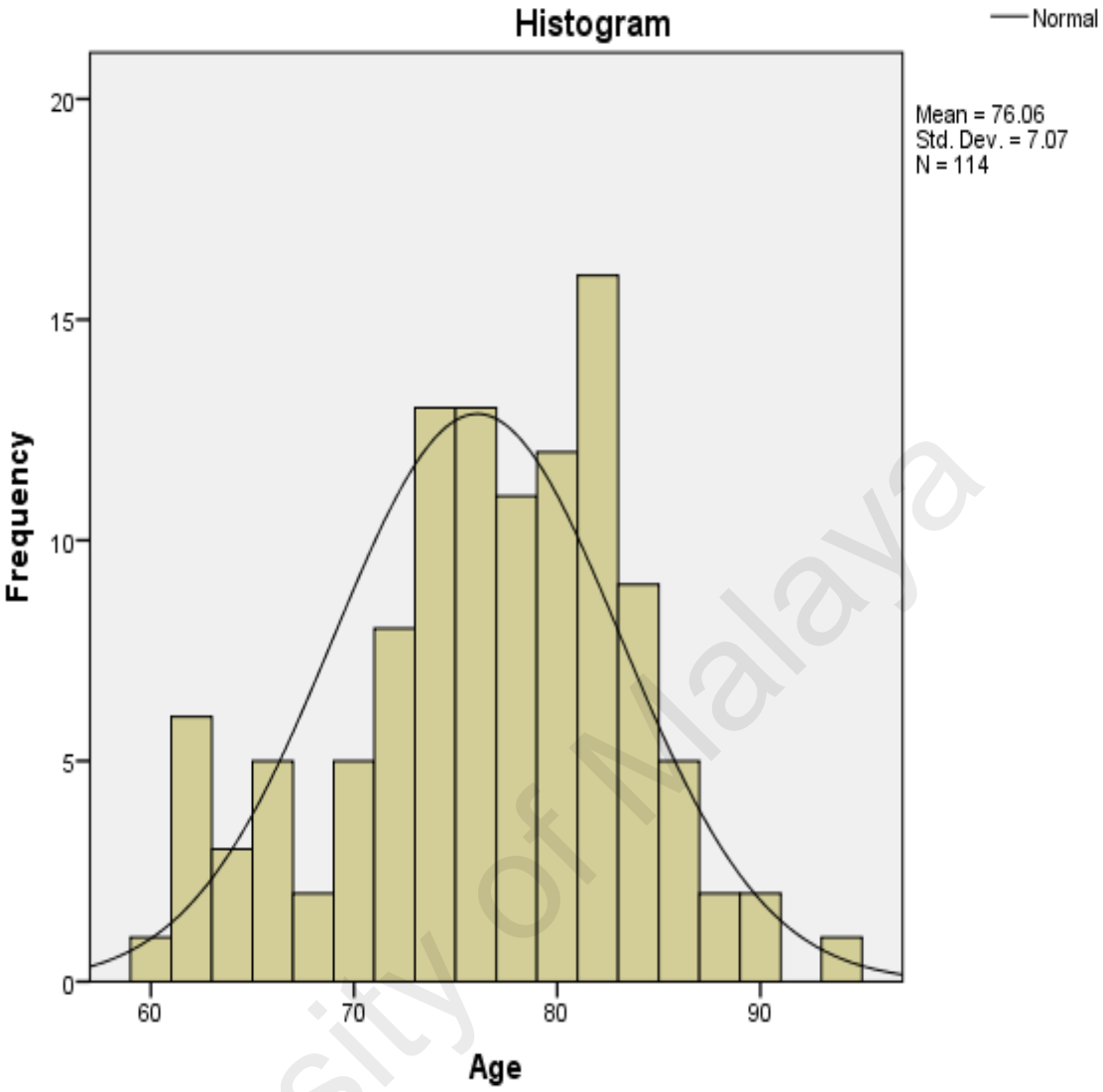


**Figure 5.1** Histogram age of study samples

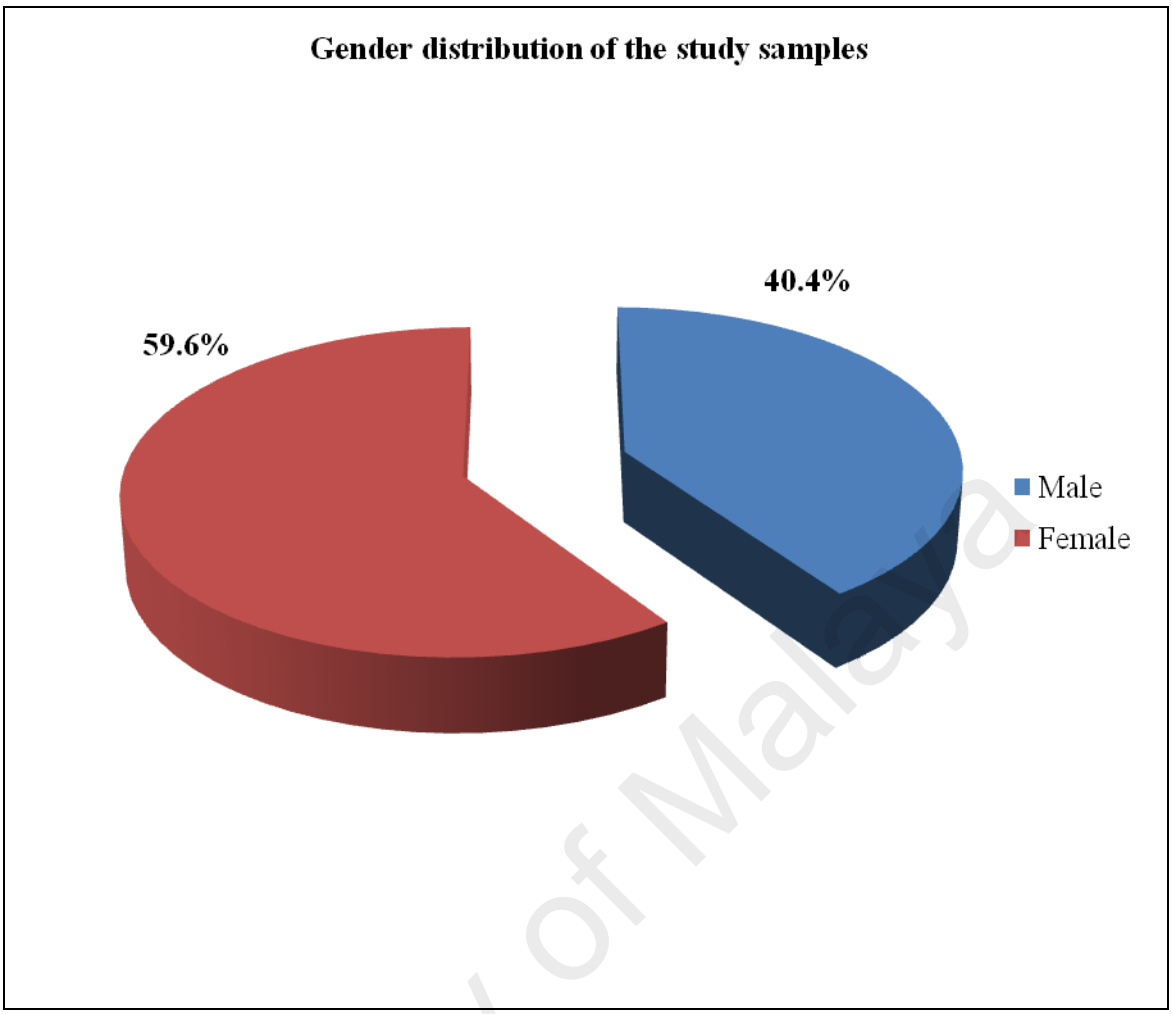


**Figure 5.2** Gender distributions of the study samples

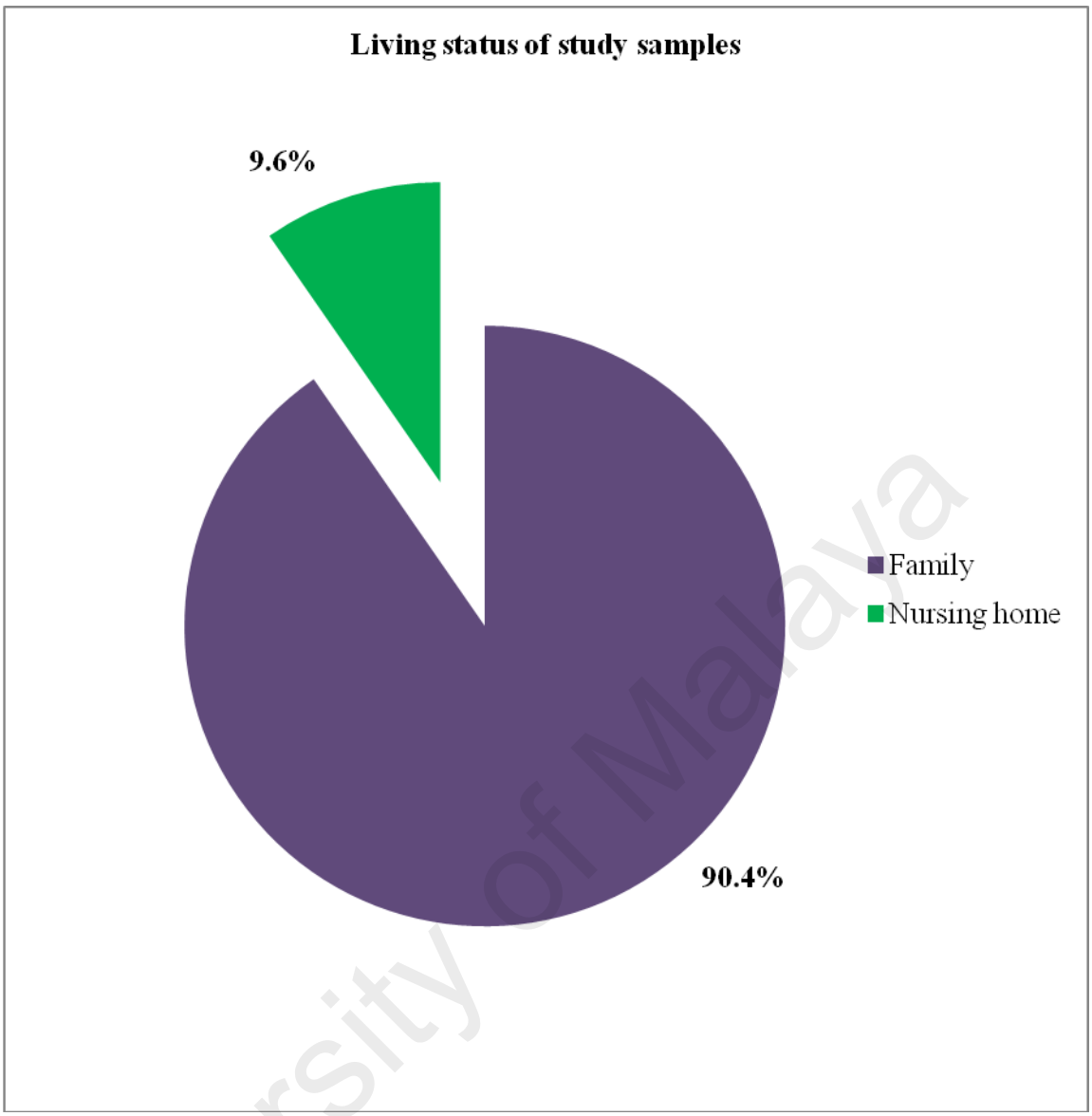


**Figure 5.3** Living status of study samples

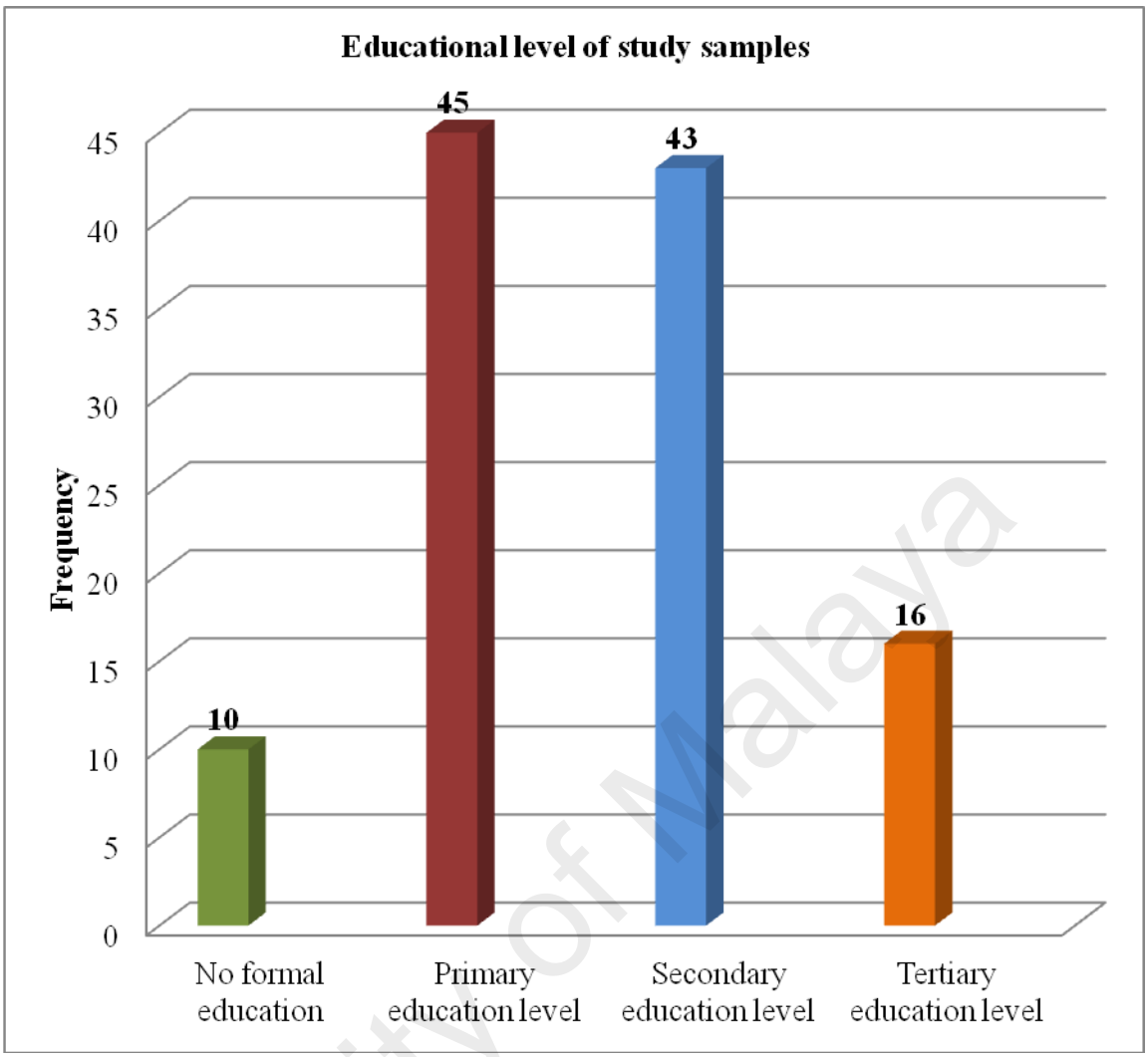


**Figure 5.4** Educational levels of study samples

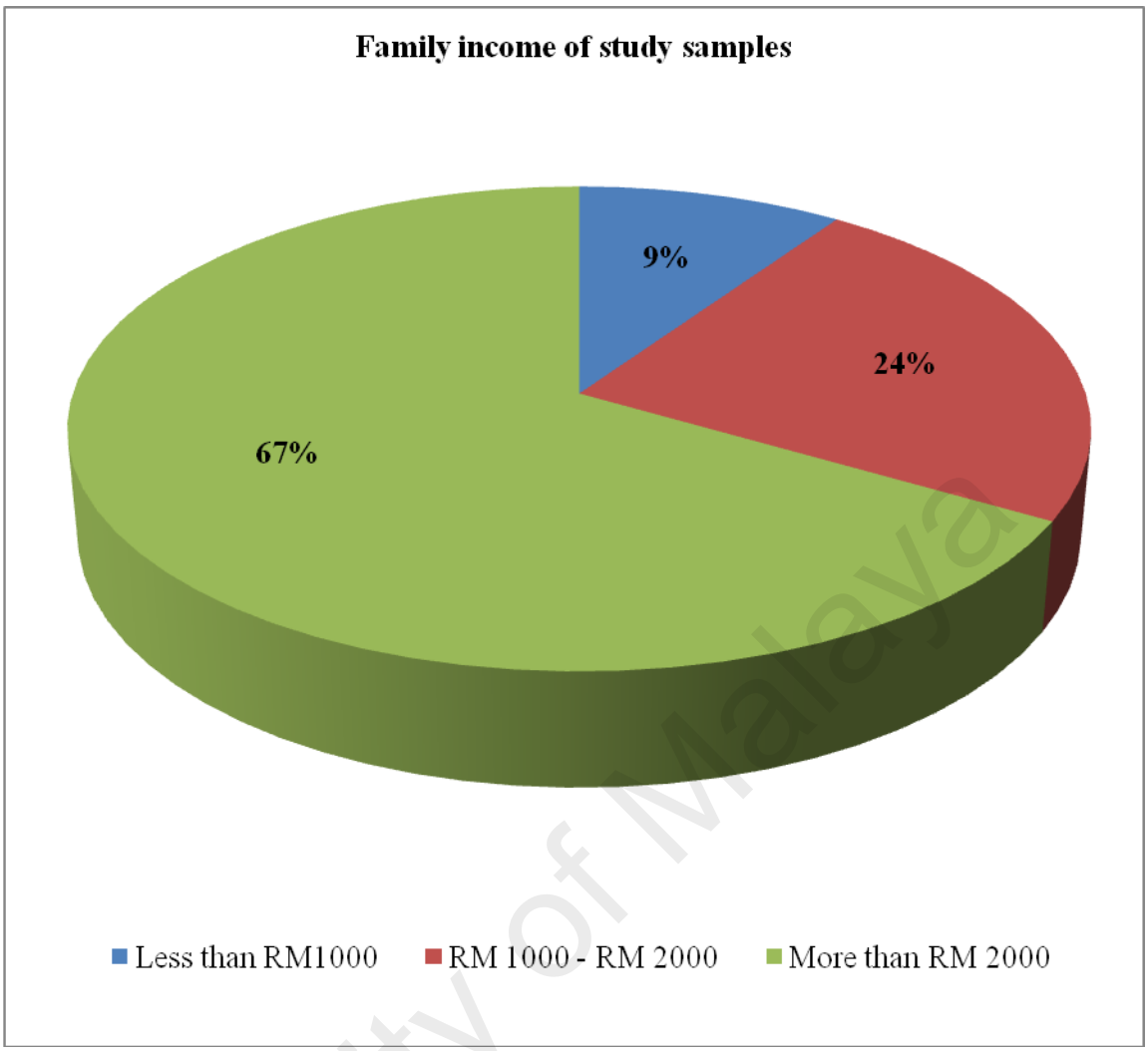


**Figure 5.5** Family incomes of study samples

## 5.2 Clinical profiles of study samples

### 5.2.1 Clinical data of study samples

Majority of the samples (77.2%) had co-morbidity of medical illness, while the remaining 22.8% had no medical co-morbidity. 9 patients (7.9%) had past psychiatry history which included bipolar disorder, schizophrenia and depression while 105 patients (92.1%) did not have any previous psychiatry history (Table 5.2).

17.5% of the study samples were diagnosed to have dementia within year 2012, whereas 63.2% of samples were diagnosed between 1 to 3 years ago and the remaining 19.3% were diagnosed more than 3 years ago (Table 5.2). Half of the study samples (50%) was diagnosed to have Dementia of Alzheimer's type, followed by 22.8% of patients with the diagnosis of vascular dementia, and 19.3% of samples were diagnosed to have mixed dementia (Alzheimer's dementia and vascular dementia) and 9 patients (7.9%) were having other type of dementia which includes 3 patients with Parkinson's disease dementia, 3 patients with Lewy Body dementia, 1 patient with fronto-temporal dementia, 1 patient with meningioma and 1 patient with frontal cyst (Figure 5.6).

Majority of the patients (92.1%) were on dementia medication such as Donepezil, Rivastigmine and/or Memantine whereas 7.9% of patients were not on any dementia medication (Figure 5.7). When looking at the number of medications that were prescribed to the patients which included the dementia medication, antipsychotics and other medications which include antidepressant, mood stabilizer and sedative hypnotics, about half of the patients (50.9%) were on single medication, 38 patients (33.3%) were

on 2 types of medications either 2 types of dementia medications or single dementia medications with either antipsychotic or sedative hypnotics and 9 patients (7.9%) were on more than 2 types of medications (Figure 5.8).

In terms of the frequency of patients being prescribed dementia medications and antipsychotic, 54 patients were prescribed Donepezil, 37 patients were on Rivastigmine, 28 patients were prescribed Memantine and 27 patients were on antipsychotic (Figure 5.9).

Majority of care givers (93.9%) did not join any support group while only small proportion of care givers joined the support group with Alzheimer's disease Foundation of Malaysia (ADFM) which accounted of 6.1% of the patients' care givers.

The summary of profiles of the study samples is shown in Table 5.2.

**Table 5.2** Descriptive characteristic of clinical data (N=114)

| Clinical profile | N (%) | Median (IQR) |
|---|---|---|
| **Medical problem** | | |
| Present | 88 (77.2) | |
| Absent | 26 (22.8) | |
| **Past psychiatry history** | | |
| Present | 9 (7.9) | |
| Absent | 105 (92.1) | |
| **Duration of diagnosis of dementia** | | |
| Less than 1 year | 20 (17.5) | |
| 1 – 3 years | 72 (63.2) | |
| More than 3 years | 22 (19.3) | |
| **Types of dementia** | | |
| Dementia of Alzheimer's type | 57 (50.0) | |
| Vascular dementia | 26 (22.8) | |
| Mixed dementia (AD & VaD) | 22 (19.3) | |
| Others | 9 (7.9) | |
| **Dementia medications** | | |
| Yes | 105 (92.1) | |
| No | 9 (7.9) | |
| **Number of medications** | | |
| No dementia medication | 9 (7.9) | |
| 1 type of medication | 58 (50.9) | |
| 2 types of medications | 38 (33.3) | |
| More than 2 types of medications | 9 (7.9) | |
| **Donepezil** | | |
| Yes | 54 (47.4) | |
| No | 60 (52.6) | |
| **Rivastigmine** | | |
| Yes | 37 (32.5) | |
| No | 77 (67.5) | |
| **Memantine** | | |
| Yes | 28 (24.6) | |
| No | 86 (75.4) | |
| **Antipsychotic** | | |
| Yes | 27 (23.7) | |
| No | 87 (76.3) | |
| **Other medications** | | |
| Yes | 19 (16.7) | |
| No | 95 (83.3) | |
| **Support group** | | |
| Yes | 7 (6.1) | |
| No | 107 (93.9) | |
| **MINI – Depressed** | | |
| Yes | 12 (10.5) | |
| No | 102 (89.5) | |
| **MMSE** | | 19.00(9) |
| **GDS score** | | 3.00 (2) |

IQR = interquartile range, AD=Alzheimer's dementia, VaD=Vascular dementia

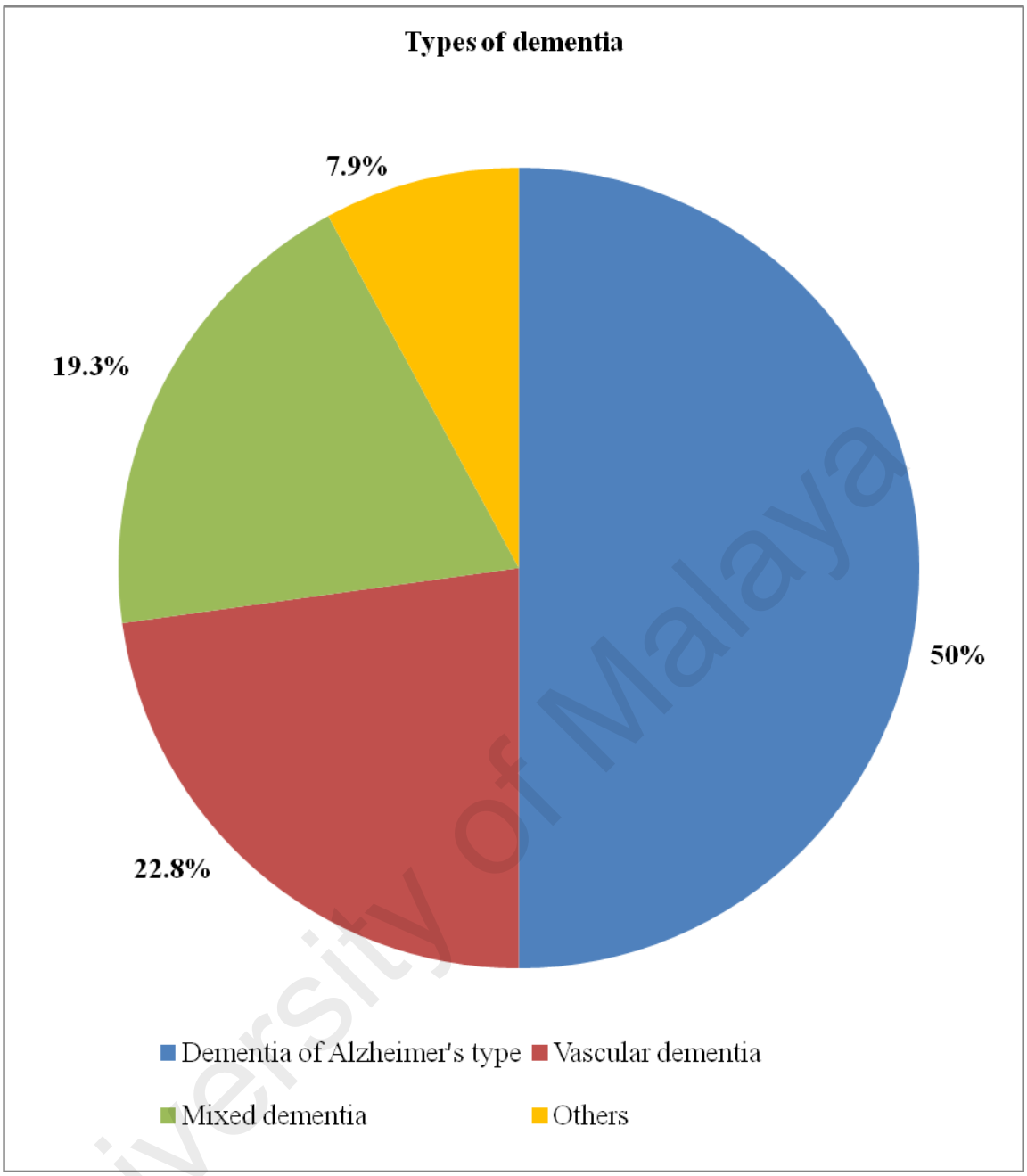


**Figure 5.6** Distribution of samples according to types of dementia

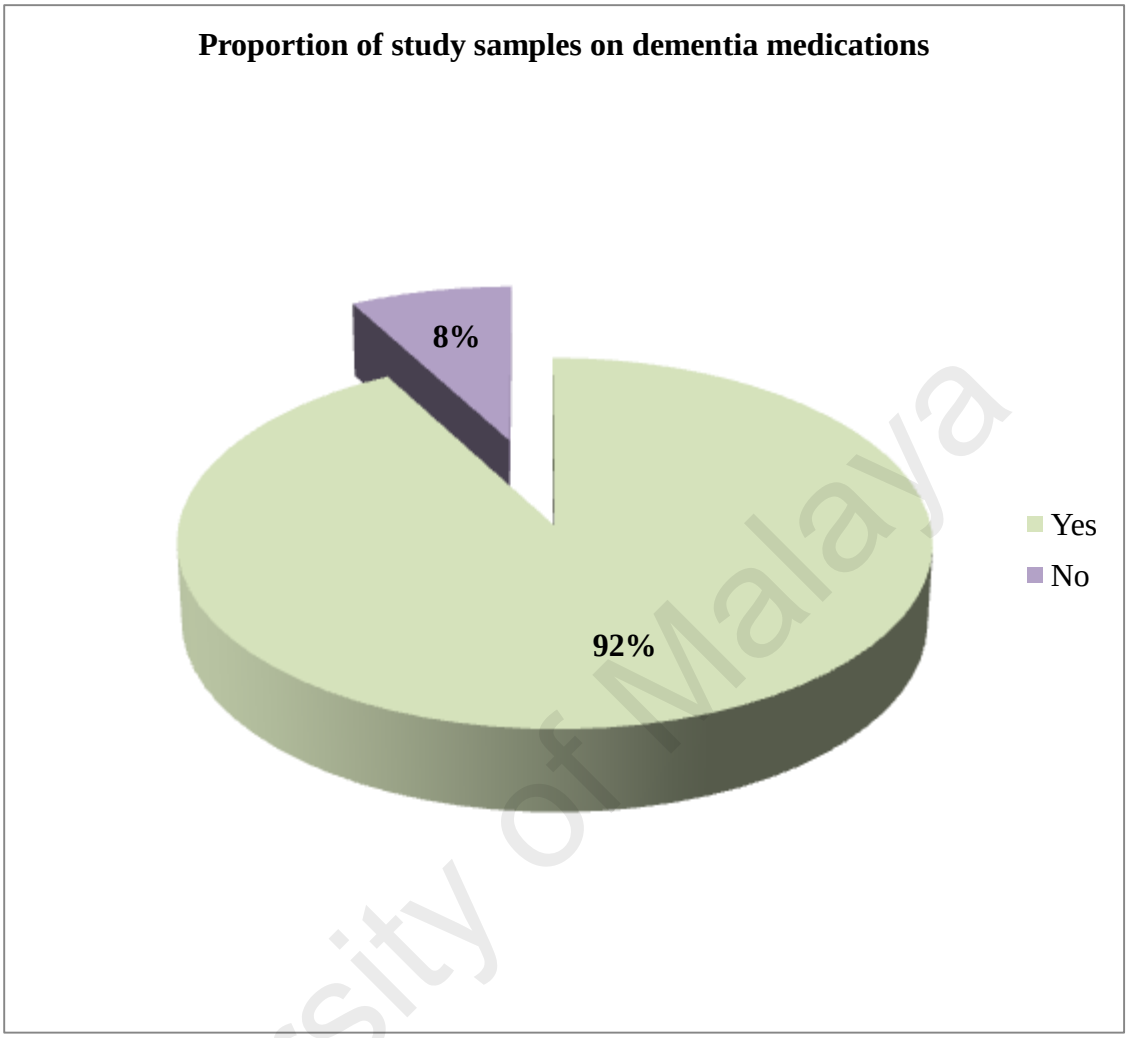


**Figure 5.7** Proportion of study samples on dementia medications

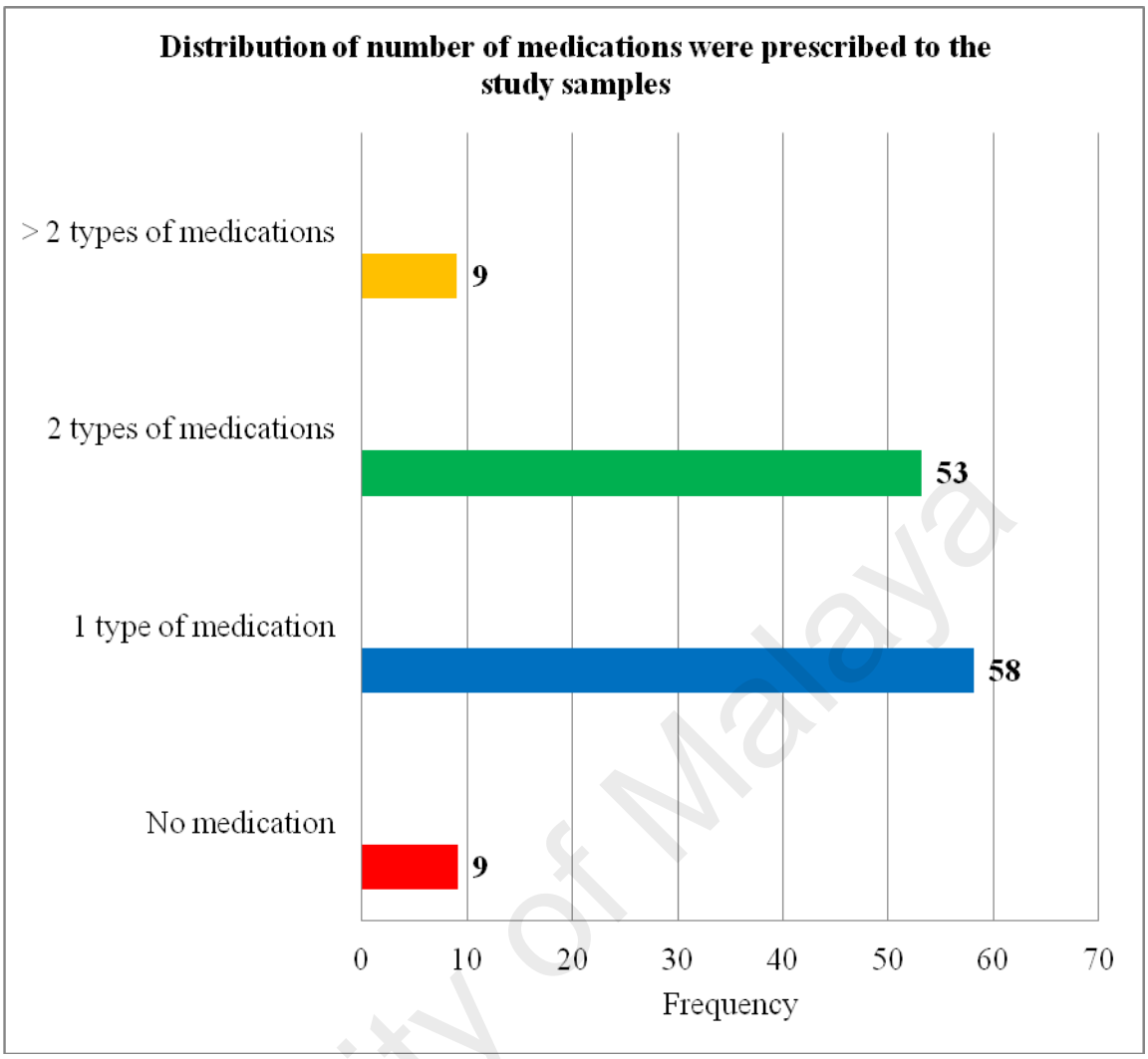


**Figure 5.8** Distribution of number of medications that were prescribed to study sample

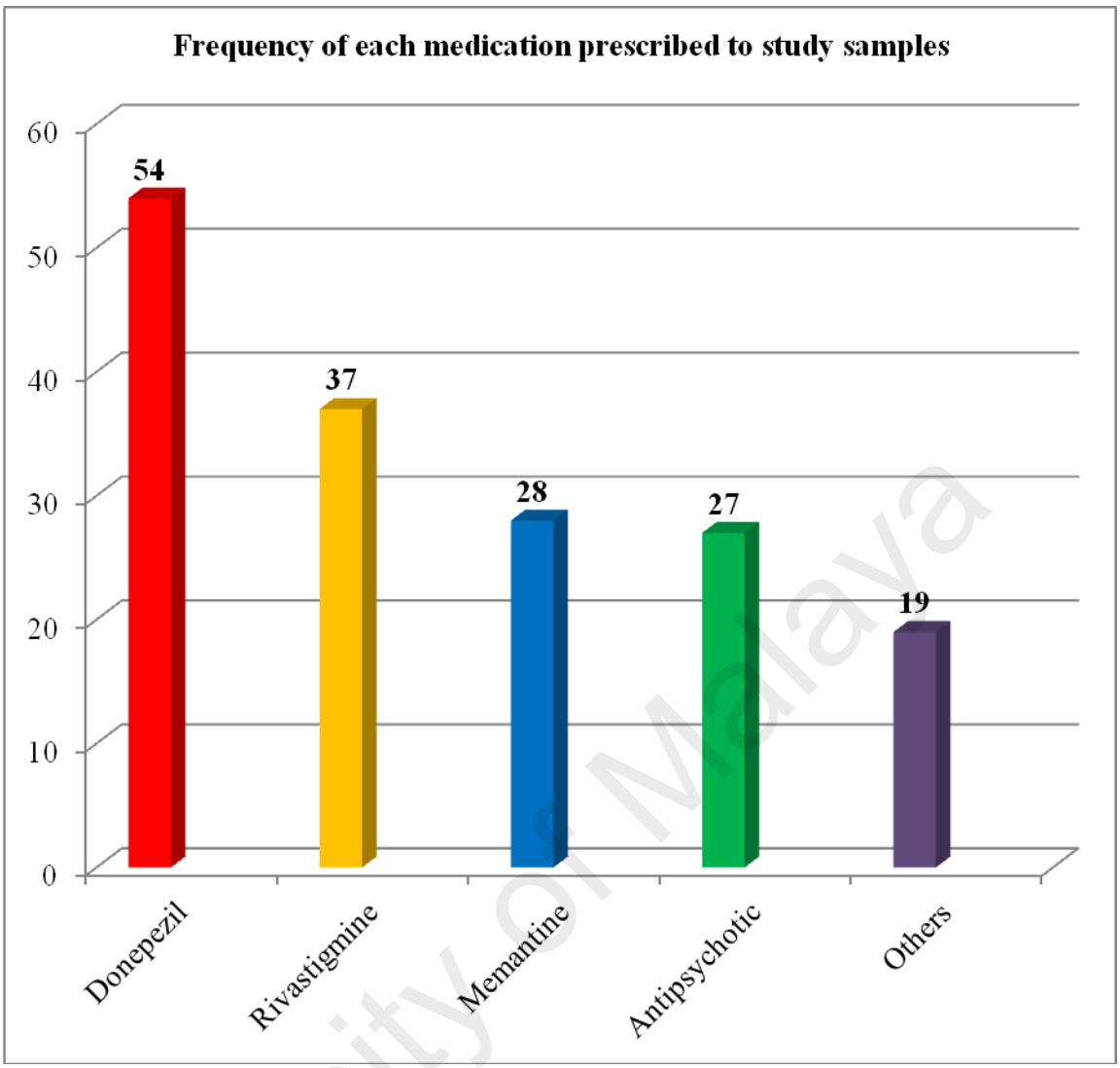


**Figure 5.9** Frequency of each medication prescribed to study samples

### 5.2.2 Mini Mental State Examination (MMSE) score and the Geriatric Depression Scale 15 items (GDS-15) score

The Mini Mental State Examination (MMSE) score for this study samples was range from 10 to 29. The MMSE score was not normally distributed based on the Kolmogorov-Smirnov test of normality, therefore the median of MMSE score was 19 with the interquartile range of 9 (Figure 5.10).

The Geriatric Depression Scale 15 items (GDS-15) score for the patients that were recruited in this study ranging from 0 to 14. The GDS scores were also not normally distributed based on the Kolmogorov-Smirnov test of normality. The median of GDS-15 score was 3 with interquartile range of 2 (Figure 5.11).

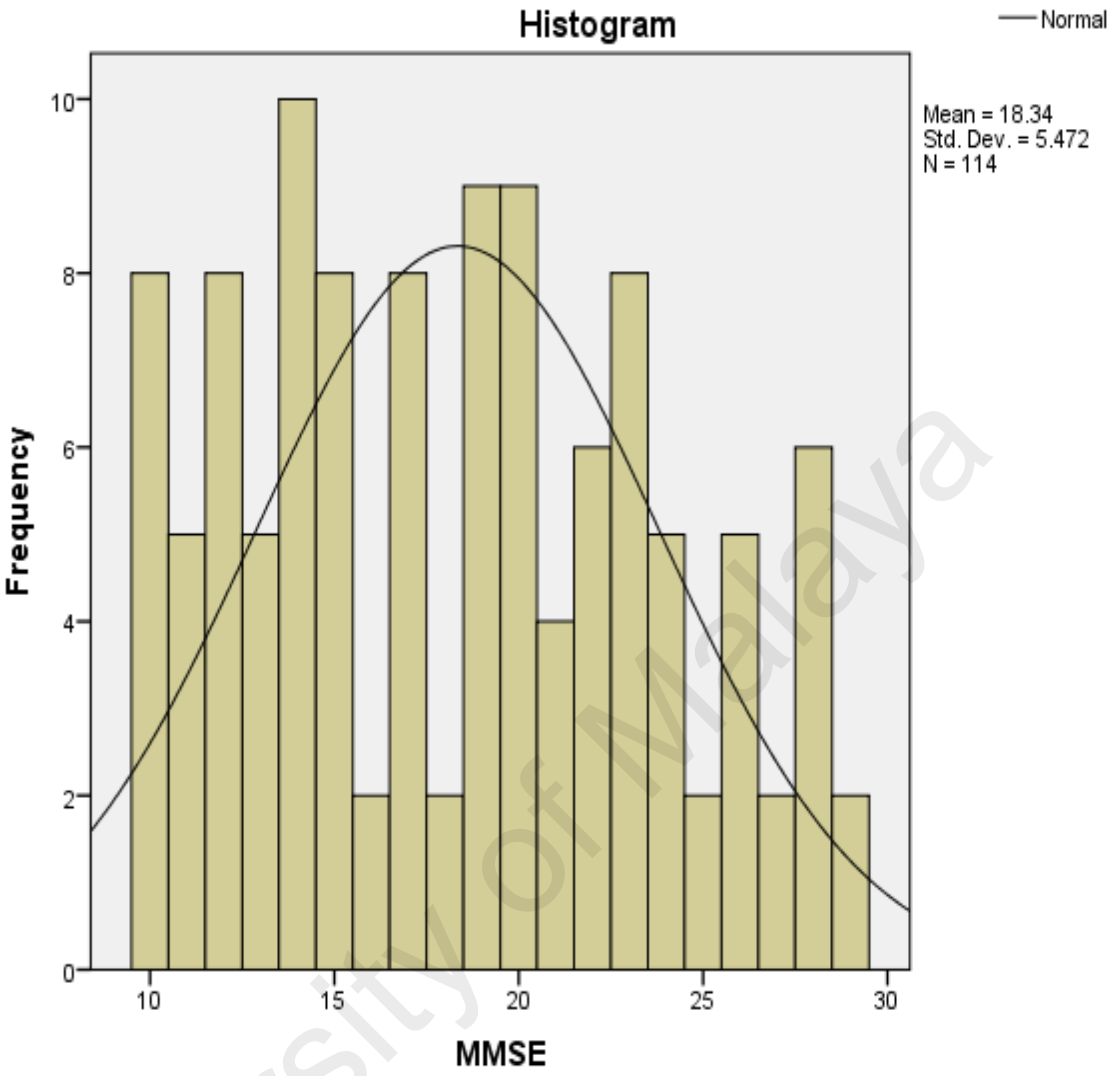


**Figure 5.10** Histogram of MMSE score

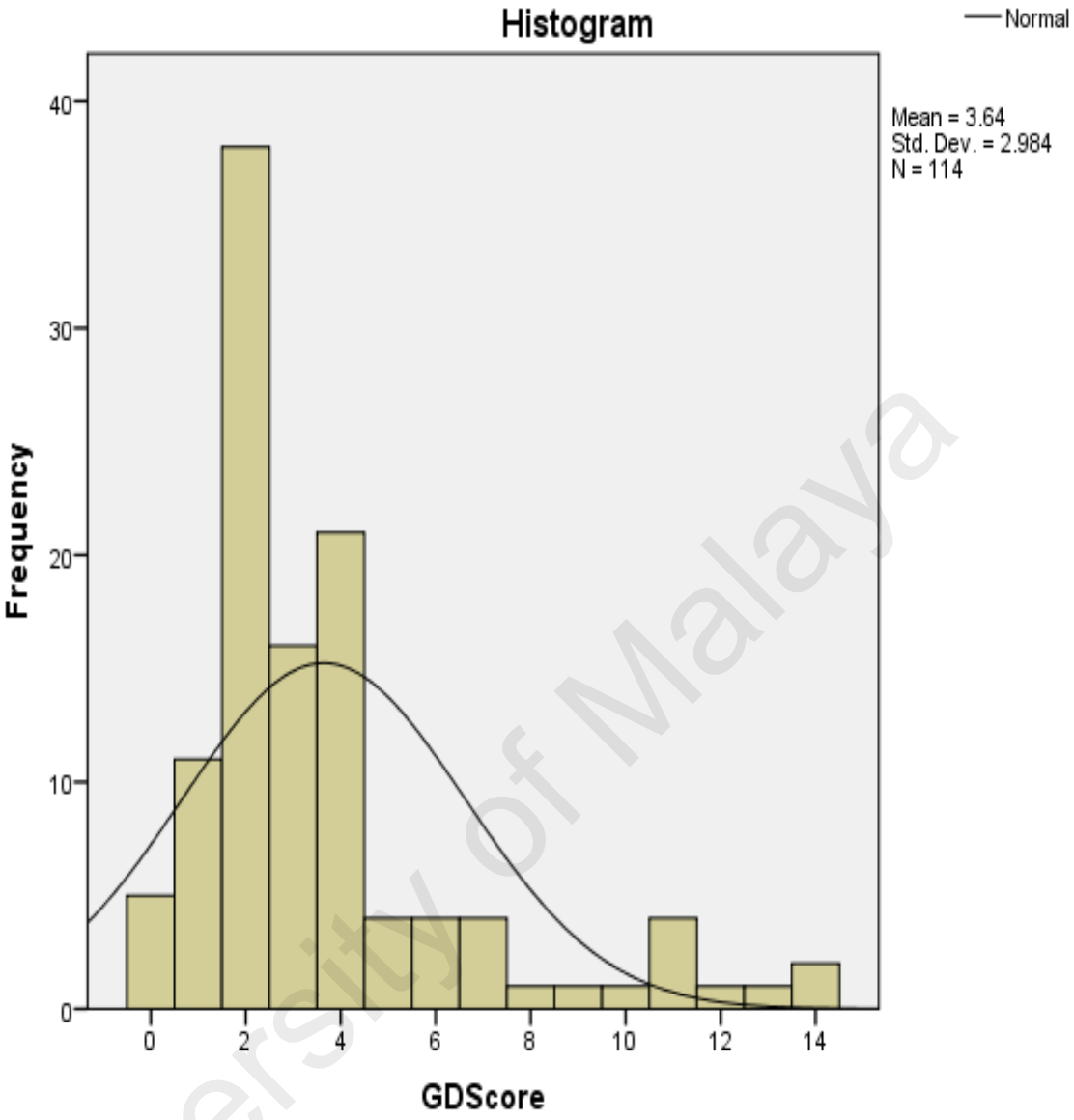


**Figure 5.11** Histogram of GDS-15 score

### 5.3 Prevalence of depression in patients with dementia

Out of the 114 study sample, 23 patients (20.2%) were found to be depressed when using Geriatric Depression Scale with cut-off point 5 and above (Figure 5.12). The patients that were found to be depressed also included those who had minor depressive symptoms when using the cut-off point 5 and above. 8 patients (14.0%) from 57 patients who has Alzheimer's disease, 7 patients (26.9%) of those who had the diagnosis of vascular dementia, while 5 (22.7%) from 22 patients with mixed dementia and 3 (33.3%) out of 9 patients who had other types of dementia were found to be depressed base on GDS-15 with cut-off 5 or more (Table 5.2; Figure 5.14).

A total of 12 patients (10.5%) were found to have major depressive disorder based on the Mini International Psychiatry Interview (M.I.N.I) (Figure 5.13). based on the type of dementia, 8.8% of patients (n=5) with Alzheimer's disease, 11.5% of patients (n=3) with vascular dementia, 9.1% of patients (n=2) diagnosed with mixed dementia and 22.2% of patients (n=2) with other types of dementia were detected to have having major depressive episode based on M.I.N.I (Table 5.2; Figure 5.15)

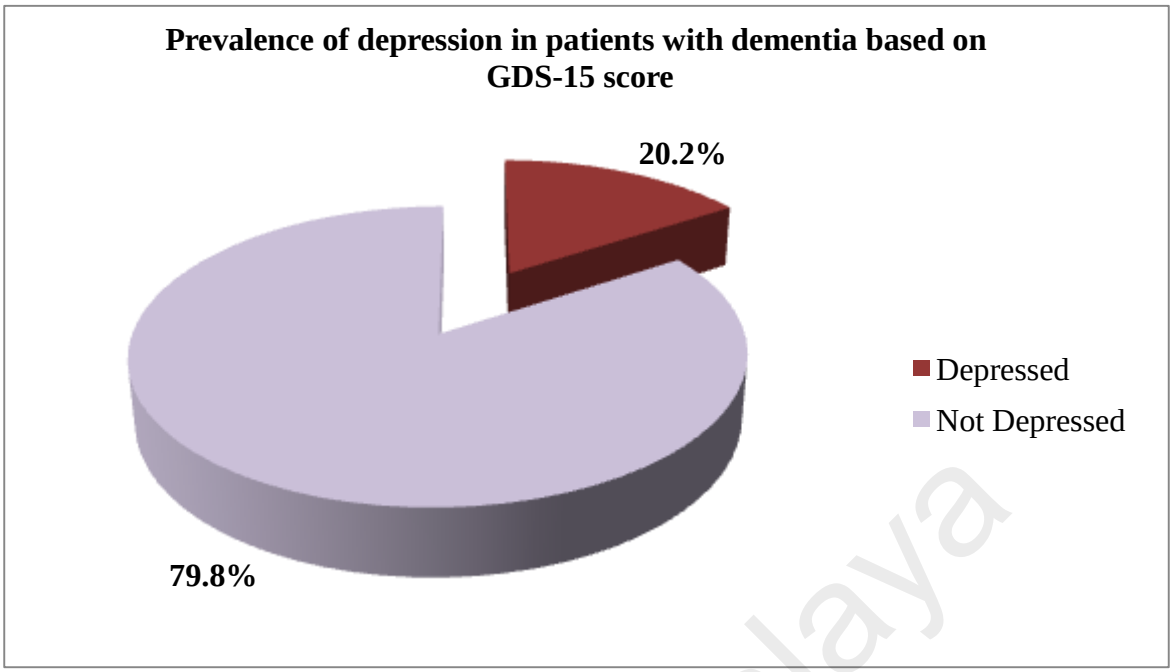


**Figure 5.12** Prevalence of depression in patients with dementia based on GDS-15 ≥ 5

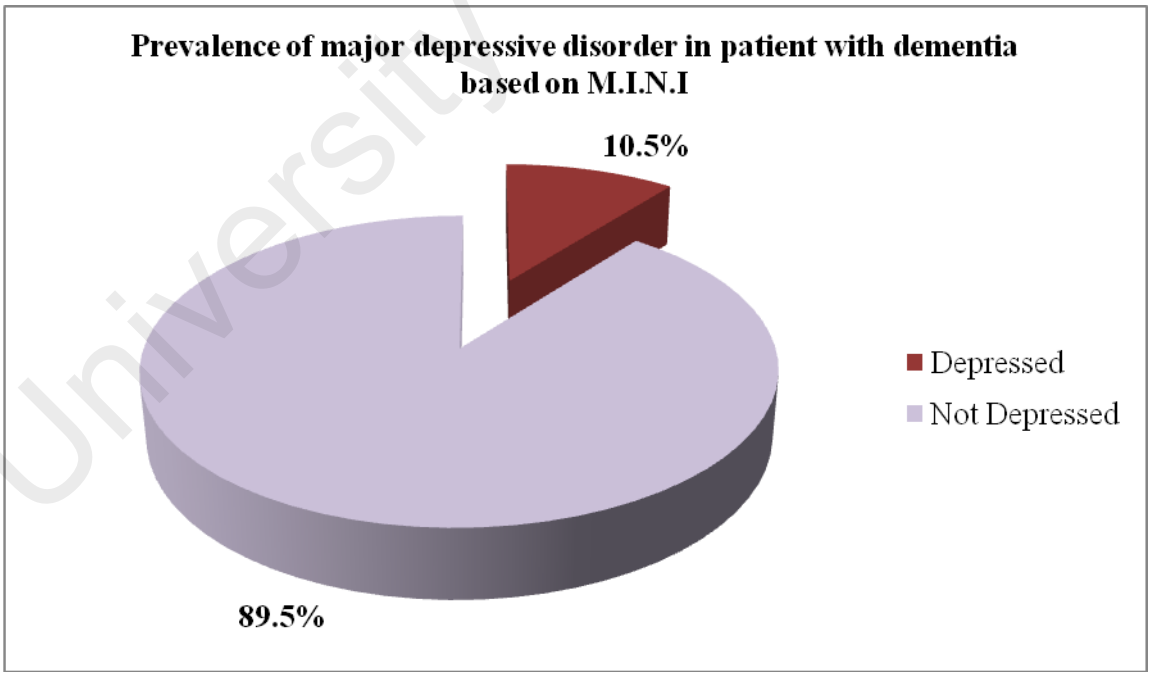


**Figure 5.13** Prevalence of major depressive disorder in patients with dementia based on M.I.N.I.

**Table 5.3** Distribution of depressed patients based on M.I.N.I and GDS-15 with cut-off point ≥ 5 according to types of dementia

| Types of dementia | GDS – Depressed n (%) | MINI – Depressed n (%) |
|---|---|---|
| Alzheimer's disease (n=57) | 8 (14.0) | 5 (8.8) |
| Vascular dementia (n=26) | 7 (26.9) | 3 (11.5) |
| Mixed dementia (n=22) | 5 (22.7) | 2 (9.1) |
| Other types of dementia (n=9) | 3 (33.3) | 2 (22.2) |

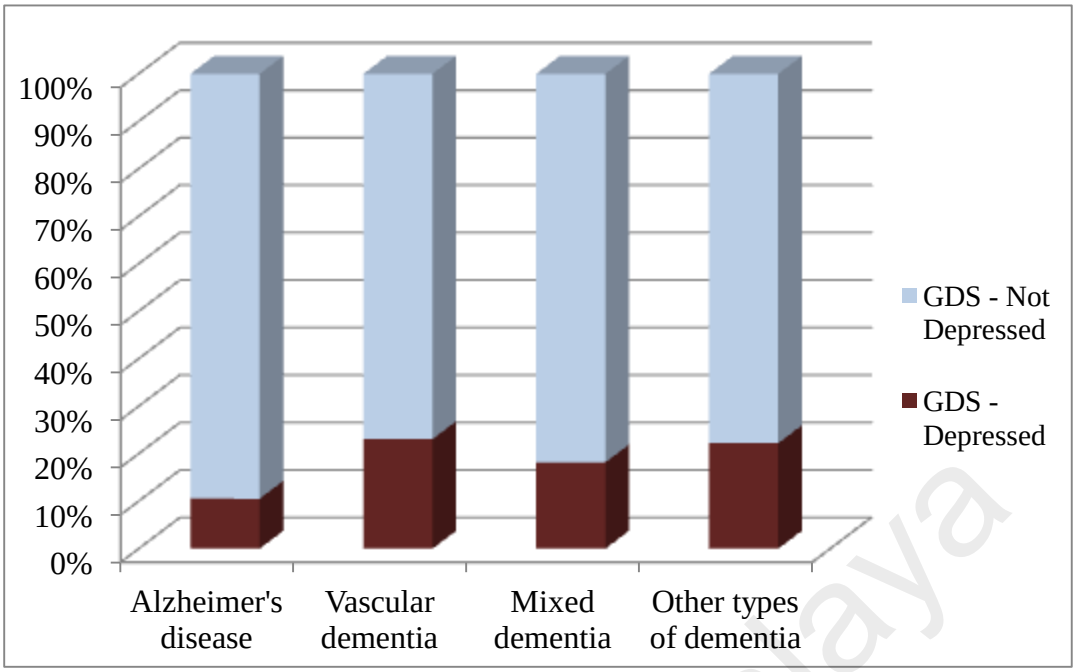


**Figure 5.14** Distribution of depressed patients based on GDS-15with cut-off ≥5 according to types of dementia

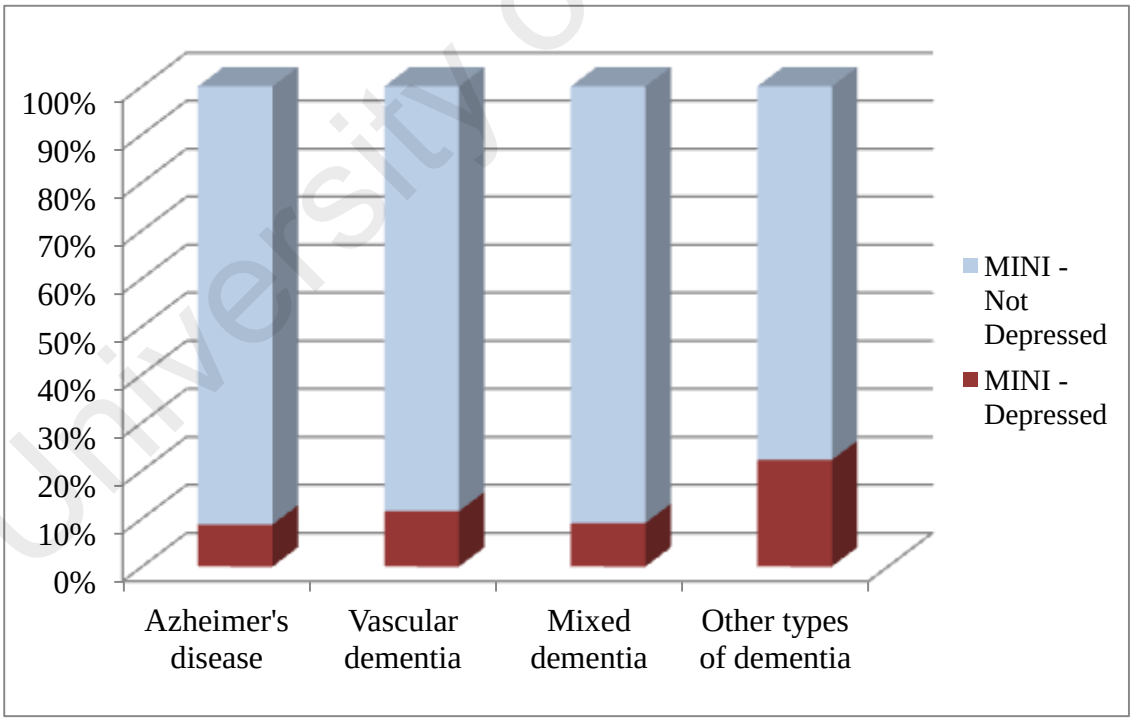


**Figure 5.15** Distribution of depressed patients based on M.I.N.I according to types of dementia

## 5.4 Association and regression

### 5.4.1 Univariate analysis of depression on Geriatric Depression Scale 15 item (GDS-15) and the socio-demographic data

All the variables were categorized into 2 groups for univariate analysis and subsequent analyses.

For the univariate analysis of GDS-15, we are using GDS as continuous data while in multivariate analysis, GDS-15 would be analyzed as categorical data with cut-off score 5 or more.

The median GDS-15 score were the same between Malays and Non Malays; those married and those who were widowed, single or divorcee and the patients with or without employment history (Table 5.4).

The median GDS-15 score were higher in patient with age less than 75 years old compared with patients aged more than 75 years old. Male patients had median score of GDS-15 higher than the female patients. Study samples that were staying in nursing home had median scored of their GDS-15 higher compared with those staying with the family.

Median score of GDS-15 in those patients with family income of more than RM 2000 were higher compared with the patients with family income of less than RM 2000. However, there were no significant associations between patient's age, gender, having children and living status with GDS-15 score.

The only socio-demographic factor that found to be significantly associated with the GDS-15 score was the educational status which the median score of patients with education level of primary school level or less (median score=3) were higher compared with those who had educational level of secondary school or higher (Median score=2) with p value of 0.023.

**Table 5.4** Univariate analysis of associated socio-demographic factors of depression based on GDS score using Mann Whitney test

| Variable | GDS | z value | p value |
|---|---|---|---|
| | Median (IQR) | | |
| **Age** | | | |
| 60 – 75 years old | 3.0 (2) | -0.685 | 0.493 |
| More than 75 years old | 2.5 (2) | | |
| **Gender** | | | |
| Male | 3.0 (2) | -0.822 | 0.411 |
| Female | 2.0(2) | | |
| **Race** | | | |
| Malays | 3.0 (3) | -0.300 | 0.764 |
| Non Malays | 3.0 (2) | | |
| **Marital status** | | | |
| Married | 3.0 (2) | -0.502 | 0.616 |
| Widow/ Divorced/Single | 3.0 (2) | | |
| **Children** | | | |
| Yes | 3.0 (2) | -0.159 | 0.874 |
| No | 2.0 (3) | | |
| **Employment History** | | | |
| Yes | 3.0 (2) | -0.333 | 0.739 |
| No | 3.0 (2) | | |
| **Living status** | | | |
| Living with family | 3.0 (2) | -1.376 | 0.169 |
| Living in nursing home | 4.0 (5) | | |
| **Education** | | | |
| Primary or lower | 3.0 (2) | -2.277 | 0.023* |
| Secondary or higher | 2.0 (2) | | |
| **Family income** | | | |
| RM 2000 or less | 2.5 (2) | -0.493 | 0.622 |
| More than RM 2000 | 3.0 (2) | | |

* p value < 0.05 is significant, IQR=Interquartile range

### 5.4.2 Univariate analysis of depression on Geriatric Depression Scale 15 item (GDS-15) and the clinical data

The median GDS-15 score were the same between the patients who were diagnosed with dementia of less or more than 1 year. Similarly for those who were prescribed with Rivastigmine and those who were not prescribed Rivastigmine and those who were on Memantine and not taking Memantine; the median GDS-15 were the same (Table 5.5).

Study samples without medical illness had median scored of their GDS-15 higher compared with those who had medical illness. The median GDS-15 score were higher in patient with past psychiatry history compared with patients without past psychiatry history. Patient with Alzheimer's dementia had median score of GDS-15 lower than the patients with other types of dementia.

Median score of GDS-15 in those patients who were on dementia medications were higher compared with the patients who were not on dementia medication. Those patients who were not on Donepezil had median score of GDS-15 higher compared with patients who were on Donepezil.

However, medical co-morbidity status, past psychiatry history, types of dementia, dementia medication and prescription of Donepezil were not found to be significantly associated with GDS-15 score.

The clinical factors that found to be significantly associated with the GDS-15 score were prescription of antipsychotic and the severity of dementia based on MMSE score. Patients who were on antipsychotic had higher median GDS-15 score (median score=3) compared with patients who were not on antipsychotic (median score=2) with p value of 0.047.

The median GDS-15 score for patients with moderate dementia were higher (median score=3) compared with mild dementia patients (median score=2) with p value of 0.001.

The univariate analysis of clinical variables with GDS-15 score is shown in Table 5.5.

**Table 5.5** Univariate analysis of associated clinical factors of depression based on GDS score using Mann Whitney test

| Variable | GDS | z value | p value |
|---|---|---|---|
| | Median (IQR) | | |
| **Medical problem** | | | |
| Present | 2.5 (2) | -1.083 | 0.279 |
| Absent | 3.0 (2) | | |
| **Past psychiatry** | | | |
| Present | 4.0 (3) | -1.410 | 0.159 |
| Absent | 3.0 (2) | | |
| **Duration of diagnosis** | | | |
| < 1 year | 3.0 (2) | -0.526 | 0.599 |
| > 1 year | 3.0 (4) | | |
| **Type of dementia** | | | |
| Alzheimer's dementia | 2.0 (2) | -0.705 | 0.481 |
| Other type of dementia | 3.0 (3) | | |
| **Dementia medication** | | | |
| Yes | 3.0 (2) | -1.319 | 0.187 |
| No | 2.0 (3) | | |
| **Number of medication** | | | |
| ≤ 1 medication | 3.0 (2) | -0.617 | 0.537 |
| ≥ 2 medications | 3.5 (4) | | |
| **Donepezil** | | | |
| Yes | 2.0 (2) | -0.860 | 0.390 |
| No | 3.0 (2) | | |
| **Rivastigmine** | | | |
| Yes | 3.0 (2) | -0.139 | 0.889 |
| No | 3.0 (2) | | |
| **Memantine** | | | |
| Yes | 3.0 (2) | -0.870 | 0.384 |
| No | 3.0 (2) | | |
| **Antipsychotic** | | | |
| Yes | 3.0 (3) | -1.983 | 0.047* |
| No | 2.0 (2) | | |
| **Support group** | | | |
| Yes | 6.0 (9) | -0.997 | 0.319 |
| No | 3.0 (2) | | |
| **Severity of dementia based on MMSE score** | 2.0 (1) | -3.277 | 0.001* |
| Mild | 3.0 (4) | | |
| Moderate | | | |

* p value < 0.05 is significant, IQR=Interquartile range

### 5.4.3 Univariate analysis of major depressive disorder based on M.I.N.I and the socio-demographic data

Among those patients age less than 75 years old, 12.5% of them were diagnosed to have major depressive disorder compared with 8.6% of those aged more than 75 years old were found to be depressed. The proportions of male and female study samples with depression were almost the same; of which 10.9% and 10.3% of male and female patients were diagnosed to have major depressive disorder respectively.

As the majority of the study samples were Non Malays, the proportion of the Non Malays that found to have depression were 11% compared with 8.7% in the Malays samples. 11.6% of the married sample had major depressive disorder while 8.9% of those who either widowed, single or divorcee had depression. The proportions of depression in samples without children were higher compared to those with children with the percentage of 12.5% and 10.4% respectively.

Prevalence of depression among the study sample that had employment history (8.8%) were lower compare with those without employment history or were housewife (17.4%) (Table 5.6).

Proportions of dementia patients who were found to have depression among the patients that were staying in nursing home were higher (27.3%) compared with the proportion of depressed patient among those who were staying with the family (8.7%).

Among the patients with education level of primary school or lower, 12.7% of them were found to be depressed. This proportion was higher compared with the proportion of depressed patient within the patients with education level of secondary school or higher which accounted of 8.5%.

There was no difference in the prevalence of depression among patients in terms of the family income (less and more than RM 2000).

None of the socio-demographic profiles above were found to be significantly associated with diagnosis of major depressive disorder in patients with dementia.

The association of the socio-demographic data with M.I.N.I is shown in the Table 5.6.

**Table 5.6** Univariate analysis of associated socio-demographic factors for depression based on MINI using Chi Square analysis

| Variable | Depression | | Chi Square | OR | p value | 95% CI |
|---|---|---|---|---|---|---|
| | Yes N (%) | No N (%) | | | | |
| **Age** | | | | | | |
| 60 – 75 years old | 7 (12.5) | 49 (87.5) | 0.455 | 1.514 | 0.500 | 0.451 – 5.086 |
| More than 75 years old | 5 (8.6) | 53 (91.4) | | | | |
| **Gender** | | | | | | |
| Male | 5 (10.9) | 41 (89.1) | - | 1.063 | 1.000 [a] | 0.316 – 3.578 |
| Female | 7 (10.3) | 61 (89.7) | | | | |
| **Race** | | | | | | |
| Malays | 2 (8.7) | 21 (91.3) | - | 0.771 | 1.000 [a] | 0.157 – 3.791 |
| Non Malays | 10 (11.0) | 81 (89.0) | | | | |
| **Marital status** | | | | | | |
| Married | 8 (11.6) | 61 (88.4) | - | 1.344 | 0.761 [a] | 0.380 – 4.757 |
| Widow/Divorced/Single | 4 (8.9) | 41 (91.1) | | | | |
| **Children** | | | | | | |
| Yes | 11 (10.4) | 95 (89.6) | - | 0.811 | 1.000 [a] | 0.091 – 7.215 |
| No | 1 (12.5) | 7 (87.5) | | | | |
| **Employment History** | | | | | | |
| Yes | 8 (8.8) | 83 (91.2) | - | 1.442 | 0.257 [a] | 0.125 – 1.679 |
| No | 4 (17.4) | 19 (82.6) | | | | |
| **Living status** | | | | | | |
| Living with family | 9 (8.7) | 94 (91.3) | - | 0.255 | 0.091 [a] | 0.057 – 1.136 |
| Living in nursing home | 3 (27.3) | 8 (72.7) | | | | |
| **Education** | | | | | | |
| Primary or lower | 7 (12.7) | 48 (87.3) | 0.547 | 1.575 | 0.460 | 0.469 – 5.291 |
| Secondary or higher | 5 (8.5) | 54 (91.5) | | | | |
| **Family income** | | | | | | |
| RM 2000 or less | 4 (10.5) | 34 (89.5) | - | 1.000 | 1.000 [a] | 0.281 – 3.557 |
| More than RM 2000 | 8 (10.5) | 68 (89.5) | | | | |

[a] Fisher exact test, OR=Odds Ratio, CI=Confidence Interval

### 5.4.4 Univariate analysis of major depressive disorder based on M.I.N.I and the clinical data

Among the study samples with medical problem, only 10.2 % of them were diagnosed to have major depressive episode based on M.I.N.I. and the percentage of depression among patients without the medical problem were about the same with 11.5%. None of the patient who had history of psychiatric illness was diagnosed to have major depressive episode while 11.4% of those who did not have previous psychiatry history diagnosed to have major depressive episode in current study.

The proportion of patients who were diagnosed with depression among those who had dementia diagnosis more than 1 year (11.7%) were higher compared with depressed patient among those who has dementia less than 1 year (5.0%).

8.8% of patients with Dementia of Alzheimer's type had depression and it was lower compared with the patients with other type of dementia which accounted of 12.3%. Among those patients without anti-dementia medications, none of the patient has depression, whereas among the patients who prescribed with dementia medications, 11.4% of the samples were diagnosed to have depression. Among those patients who were prescribed more than one medications, 11.1 % of them had depression while 10.4% of those prescribed 1 medication or no medication were diagnosed to have depression.

Among the patients who were prescribed with medications and were diagnosed to have depression were as the following; 9.3% from those who were on Donepezil, 8.1% of those who were taking Rivastigmine , 17.9% of samples taking Memantine and 14.8% from patients who were on antipsychotic.

Among the patients whom their caregivers joined support group, 28.6% of them were diagnosed to have major depressive disorder based on M.I.N.I, while those patients whom their caregivers who did not join any support group about 9.3% of them were diagnosed to be depressed.

Among the patients with moderate dementia, 15.4% of then had depression and this figure was higher compared with patients with mild dementia who only 4.1% were diagnosed to be depressed.

None of the clinical profiles above were found to be significantly associated with diagnosis of major depressive disorder in patients with dementia.

The association of the clinical data with M.I.N.I is shown in the Table 5.7.

**Table 5.7** Univariate analysis of associated clinical factors for depression based on MINI using Chi Square analysis

| Variable | Depression | | Chi Square | OR | p value | 95% CI |
|---|---|---|---|---|---|---|
| | Yes N (%) | No N (%) | | | | |
| **Medical problem** | | | | | | |
| Present | 9 (10.2) | 79 (89.8) | - | 0.873 | 1.000 [a] | 0.281 – 3.495 |
| Absent | 3 (11.5) | 23 (88.5) | | | | |
| **Past psychiatry** | | | | | | |
| Present | 0 (0.0) | 9 (100) | - | 1.129 | 0.594 [a] | 1.054 – 1.209 |
| Absent | 12 (11.4) | 93 (88.6) | | | | |
| **Duration of diagnosis** | | | | | | |
| < 1 year | 1 (5.0) | 19 (95.0) | - | 0.397 | 0.689 [a] | 0.048 – 3.266 |
| > 1 year | 11 (11.7) | 83 (88.3) | | | | |
| **Type of dementia** | | | | | | |
| Alzheimer's dementia | 5 (8.8) | 52 (91.2) | 0.373 | 0.687 | 0.542 | 0.204 – 2.307 |
| Other type of dementia | 7 (12.3) | 50 (87.7) | | | | |
| **Dementia medication** | | | | | | |
| Yes | 12 (11.4) | 93 (88.6) | - | 0.886 | 0.594 [a] | 0.827 – 0.949 |
| No | 0 (0.0) | 9 (100) | | | | |
| **No of medication** | | | | | | |
| ≤ 1 medication | 10 (10.4) | 86 (89.6) | - | 0.930 | 1.000 [a] | 0.186 – 4.650 |
| ≥ 2 medications | 2 (11.1) | 16 (88.9) | | | | |
| **Donepezil** | | | | | | |
| Yes | 5 (9.3) | 49 (90.7) | 0.175 | 0.773 | 0.676 | 0.230 – 2.595 |
| No | 7 (11.7) | 53 (88.3) | | | | |
| **Rivastigmine** | | | | | | |
| Yes | 3 (8.1) | 34 (91.9) | - | 0.667 | 0.748 [a] | 0.169 – 2.623 |
| No | 9 (11.7) | 68 (88.3) | | | | |
| **Memantine** | | | | | | |
| Yes | 5 (17.9) | 23 (82.1) | - | 2.453 | 0.164 [a] | 0.711 – 8.461 |
| No | 7 (8.1) | 79 (91.9) | | | | |
| **Antipsychotic** | | | | | | |
| Yes | 4 (14.8) | 23 (85.2) | - | 1.717 | 0.474 [a] | 0.474 – 6.220 |
| No | 8 (8.2) | 79 (90.8) | | | | |
| **Support group** | | | | | | |
| Yes | 2 (28.6) | 5 (71.5) | - | 3.880 | 0.158 [a] | 0.665 – 22.650 |
| No | 10 (9.3) | 97 (90.7) | | | | |
| **Severity of dementia based on MMSE score** | | | | | | |
| Mild | 2 (4.1) | 47 (97.9) | 3.790 | 4.273 | 0.052 | 0.891 – 20.482 |
| Moderate | 10 (15.4) | 55 (84.6) | | | | |

[a] Fisher exact test, OR=Odds Ratio, CI=Confidence Interval

### 5.4.5 Multivariate analysis of depression based on Geriatric Depression Scale 15 items (GDS-15) score and the socio-demographic and clinical variables

In multivariate analysis, we only proceeded for GDS-15 and not MINI as no significant finding with the variables when using MINI in the univariate analysis. We analyzed the GDS-15 as categorical data with score of 5 or more would be categorized as depressed. The next step proceeded with the significant variables in the univariate analysis as well as the variables which were possible confounders were included into the multivariate analysis of depression using logistic regression with enter method.

Logistic regression analysis showed that after adjustment for age, gender, marital status, level of education, living status, duration of diagnosis, dementia medication and antipsychotic prescription, severity of dementia were significantly associated with depression based on GDS-15. The patients with moderate dementia based on MMSE score of 10 to 19 is 6 times more likely to have depression as compared to patients with mild dementia after adjusting for age, gender, marital status, level of education, living status, duration of diagnosis, dementia medication and antipsychotic prescription with p value of 0.006 (CI=1.661-20.747).

The Multivariate analysis using logistic regression is shown in Table 5.8.

**Table 5.8** Multivariate analysis of relationship between socio-demographic and clinical variables with depression based on GDS-15 cut-off ≥ 5 using logistic regression

| | B | S.E. | Wald | df | Sig. | Exp (B) | 95% C.I.for EXP(B) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower | Upper |
| Age | -0.593 | 0.512 | 1.343 | 1 | 0.246 | 0.552 | 0.203 | 1.507 |
| Gender | -0.485 | 0.573 | 0.715 | 1 | 0.398 | 0.616 | 0.200 | 1.893 |
| Marital status | -0.013 | 0.586 | 0.000 | 1 | 0.982 | 0.987 | 0.313 | 3.110 |
| Educational status | -0.438 | 0.540 | 0.657 | 1 | 0.418 | 0.646 | 0.224 | 1.860 |
| Living status | -0.062 | 0.825 | 0.006 | 1 | 0.940 | 0.940 | 0.187 | 4.735 |
| Duration of diagnosis | 0.668 | 0.590 | 1.280 | 1 | 0.258 | 1.950 | 0.613 | 6.198 |
| Dementia medications | 0.336 | 1.161 | 0.084 | 1 | 0.772 | 1.400 | 0.144 | 13.624 |
| Antipsychotic | 0.332 | 0.572 | 0.337 | 1 | 0.561 | 1.394 | 0.455 | 4.273 |
| Severity of dementia | 1.770 | 0.644 | 7.550 | 1 | 0.006* | 5.870 | 1.661 | 20.747 |
| Constant | -2.355 | 1.307 | 3.248 | 1 | 0.071 | 0.095 | | |

* p value < 0.05 is significant, B=regression coefficient, S.E=Standard Error, df=degree of freedom, Exp(B)= Exponential Value of Regression Coefficient, C.I=confidence interval

## 5.5 Analysis of correlation of Geriatric Depression Scale 15 item (GDS-15) score with Mini Mental State Examination (MMSE) score

As univariate and multivariate analysis showed that there was significant association between Geriatric Depression Scale 15 item (GDS-15) score and Mini Mental State Examination score, we then proceeded with analysis of correlation using Spearman correlation test.

When using analysis of correlation, we found that GDS-15 score and MMSE score was negatively correlated with Pearson's Correlation Coefficient, r of -0.335 and p value of less than 0.01 (Table 5.9). This suggested that the patient who scored lower in MMSE would have higher GDS-15 score.

**Table 5.9** Correlation of Geriatric Depression Scale 15 items (GDS-15) score with Mini Mental State Examination score using Spearman correlation

| | | | MMSE | GDS |
|---|---|---|---|---|
| Spearman's rho | MMSE | Correlation Coefficient | 1.000 | -0.335** |
| | | Sig. (2-tailed) | | p<0.01 |
| | GDS | Correlation Coefficient | -0.335** | 1.000 |
| | | Sig. (2-tailed) | p<0.01 | |

**. Correlation is significant at the 0.01 level (2-tailed)
GDS=Geriatric Depression Scale
MMSE=Mini Mental State Examination

## 5.6 Analysis of depressive symptoms based on Geriatric Depression Scale 15 items (GDS-15) between mild and moderate dementia

We had proceeded with analysis of each item in GDS-15 with score 1 and then we had made comparison between the mild and moderate dementia patients based on MMSE score. We had analyzed this association using Chi square test.

The proportions of patient with moderate dementia that score 1 were higher compared with the patients with mild dementia who score 1 in every question or item of GDS-15 except for item 11. Only 4.1% of patients with mild dementia score 1 in item 11 which is "Do you think it is wonderful to be alive now?" whereas 3.1% of patients with moderate dementia score 1 in that item; however it was not found to significantly difference (Table 5.10).

More than half of the study samples score 1 in item 2, 9 and 10; with 78 patients (68.4%) for item 2 ("Have you drop many of your activities and interest?"), 78 patients (68.4%) for item 9 ("Do you prefer to stay at home, rather than going out and do new things?") and 71 patients (62.3%) for item 10 ("Do you feel you have problem with memory than most?").

The item 2 (p=0.002, CI=0.124 - 0.646) , item 6 ("Are you afraid that something bad is going to happen to you?") (p=0.033, CI=0.044 - 0.991), item 9 (p=0.024, CI=0.178 - 0.897), item 10 (p=0.031, CI=0.198 – 0.933) and item 13 ("Do you feel full of

energy?") (p=0.036, CI=0.205 – 0.955) are the items in GDS-15 that was found to be significantly scored 1 by patients with moderate dementia compared with the patients with mild dementia.

Summary of the Chi square analysis is shown in Table 5.10.

**Table 5.10** Comparing depressive symptoms based on Geriatric Depression Scale 15 items (GDS-15) between patient with mild and moderate dementia using Chi Square analysis

| Geriatric Depression Scale | MMSE | | Chi Square | p value | 95% CI |
|---|---|---|---|---|---|
| | Mild (N=49) N (%) | Moderate (N=65) N (%) | | | |
| Item 1 | 2 (4.1) | 4 (6.2) | - | 0.698[a] | 0.114 – 3.695 |
| Item 2 | 26 (53.1) | 52 (80.0) | 9.384 | 0.002* | 0.124 – 0.646 |
| Item 3 | 3 (6.1) | 11 (16.9) | 3.025 | 0.082 | 0.084 – 1.218 |
| Item 4 | 9 (18.4) | 16 (24.6) | 0.637 | 0.425 | 0.275 – 1.724 |
| Item 5 | 5 (10.2) | 9 (13.8) | 0.344 | 0.558 | 0.221 – 2.261 |
| Item 6 | 2 (4.1) | 11 (16.9) | 4.560 | 0.033* | 0.044 – 0.991 |
| Item 7 | 3 (6.1) | 6 (9.2) | - | 0.730[a] | 0.152 – 2.703 |
| Item 8 | 3 (6.1) | 10 (15.4) | 2.372 | 0.124 | 0.093 – 1.381 |
| Item 9 | 28 (57.1) | 50 (76.9) | 5.059 | 0.024* | 0.178 – 0.897 |
| Item 10 | 25 (51.0) | 46 (70.8) | 4.638 | 0.031* | 0.198 – 0.933 |
| Item 11 | 2 (4.1) | 2 (3.1) | - | 1.000[a] | 0.182 – 9.865 |
| Item 12 | 2 (4.1) | 8 (12.3) | - | 0.184[a] | 0.061 – 1.497 |
| Item 13 | 16 (32.7) | 34 (52.3) | 4.383 | 0.036* | 0.205 – 0.955 |
| Item 14 | 2 (4.1) | 9 (13.8) | - | 0.112[a] | 0.055 – 1.286 |
| Item 15 | 8 (16.3) | 18 (27.7) | 2.050 | 0.152 | 0.201 – 1.294 |

[a] Fisher exact test, * p value < 0.05 is significant, OR=Odds Ratio, CI=Confidence Interval, MMSE=Mini Mental State Examination

# CHAPTER 6 DISCUSSION

## 6. DISCUSSION

The main objective of this study is to determine the prevalence of depression among patients with dementia attending outpatient psychogeriatric or memory clinic in Kuala Lumpur Hospital and memory clinic in University Malaya Medical Centre during the period of study from September 2012 till mid January 2013. Apart from that, the other aim of this study is to determine the relationship between the socio-demographic and clinical factors of the patients with dementia that associated with depression.

In this study, we used M.I.N.I and GDS-15 to determine the prevalence of depression. As far as we know, there was no study looking into the prevalence of depression specifically in dementia patients in our local setting. We used GDS-15 as it is shorter version of the GDS with 30 items and it is user friendly especially for the elderly that have physical illness and short attention span, with only 15 questions yes or no answer that only take short time to complete. The Geriatric Depression Scale has been showed to be able to capture the depression in patients with mild to moderate dementia (Feher *et al*., 1992; Ward *et al*., 1994; Lach *et al*., 2010; Lopez *et al*., 2010). Apart from that, Malay version GDS had already been validated in our elderly population. M.I.N.I is used as a diagnostic tool that based on DSM-IV criteria to diagnosed depression and it is sufficient enough without any modification to diagnose depression in dementia patient based on studies mention in the earlier chapter (Engedal *et al*., 2011; Starkstein *et al*., 2011). We discussed further about the findings of our study and also compared the findings with other similar studies that were done before in this chapter.

The data on the prevalence of depression in patient with dementia and the study on the associated demographic and clinical factors would benefit the policy maker and would help the health service provider to improve the service and health care of the elderly with dementia to assists them to live life to the fullest and add life to their years.

### 6.1 Prevalence of depression based on GDS-15 with cut-off ≥ 5

The prevalence of depression in this study when using GDS-15 with cut-off point 5 and more was 20.2%. The prevalence of depression based on GDS-15 was higher as compared with the prevalence of depression based on MINI as GDS with cut-off 5 and above will detect all clinically significant depression not only those who with major depression (Teh & Hasanah, 2004).

The prevalence of depression in patients with dementia in current study was comparable with a study by Kaup and colleagues that found that prevalence of depression in patient with dementia was 23.6% (Kaup *et al*., 2007). While in a study by Kales and her colleague, the prevalence of depression was 52.7% of 55 patients with dementia and this prevalence is higher compare with the current study but this study was done in those patients staying in nursing home that might influence the higher prevalence of depression in patients with dementia in their study.

If we were to see the prevalence of depression using GDS-15 according to the type of dementia, the depression was more prevalent in vascular dementia as compared with Alzheimer's disease and mixed dementia in current study. 26.9% of those who had the

diagnosis of vascular dementia were having depression as compared to 14.0% in patients with Alzheimer's disease and 22.7% of patients with mixed dementia.

### 6.2 Prevalence of major depressive disorder based on M.I.N.I

The prevalence of major depressive disorder based on M.I.N.I in this study was 10.5% (n=12) from 114 study samples. For each type of dementia, 8.8% of patients (n=5) with Alzheimer's disease, 11.5% of patients (n=3) with vascular dementia, 9.1% of patients (n=2) diagnosed with mixed dementia and 22.2% of patients (n=2) with other types of dementia were having major depressive disorder based on M.I.N.I

Prevalence of depression in our study was slightly higher than the study by Ballard and his team who found that 8% of the patients with dementia attending memory clinic had depression (Ballard *et al*., 1996). This difference was due to different in tools use in the study by Ballard and his team that use Cornell Scale for Depression in Dementia which is more comprehensive but our study used M.I.N.I. as the tool to diagnose depression. In a cross sectional study of prevalence of depression in older adult with dementia living in low- and middle-income countries, 12.4% of subjects with dementia were having depression which is comparable with the findings of our study (Andreasen, Lonnroos & Von Euler-Chelpin, 2013). The prevalence of depression in current study was lower compared with study by Lyketsos and colleagues on patients with Alzheimer's disease in an outpatient setting which found that 22% of patients were having major depression based on DSM-IV diagnosis (Lyketsos *et al*., 1997). The higher prevalence in the study by Lyketsos and colleagues (1997) was due to inclusion of patients with severe dementia that were not included in current study.

A review by Enache and colleagues (2011) found that prevalence of depression ranging from 20 to 30% of patients with Alzheimer's disease and higher in other type of dementia which is higher compare with this study. The other studies that used DSM-IV criteria to define depression also were having higher prevalence compared to the current study which found that the prevalence of depression in patient with dementia were ranging from 19% to 38.9% which are higher than prevalence that was found in current study (Verkaik *et al*., 2009; Starkstein *et al*., 2005; Barca *et al*., 2012; Porta-Etessam *et al*., 2011).

In a study that looked into the prevalence of depression in patients with Alzheimer's disease and vascular dementia, it was found that the prevalence of depression in patient with Alzheimer's disease was 10.2% while depression in patient with vascular dementia was 20.4%; which was about the same with the prevalence of depression in Alzheimer's disease patient in this study and almost double as compared with this study proportion of depressed patients with vascular dementia (Park *et al*., 2007).

The prevalence of depression based on DSM-IV criteria in patient with Alzheimer's disease was 57% and vascular dementia was 86% in the community based study by Bowirrat and colleagues and this prevalence was much higher compared to our current study with 8.8% and 11.5% of subjects with Alzheimer's Disease and vascular dementia diagnosed to have depression respectively (Bowirrat *et al*., 2006). This large different was due to the setting of the study by Bowirrat and colleagues (2006) which was done in community setting. Their initial subjects that being interviewed were 823 which could capture more caseness with their large number of subjects being evaluated hence contributed to much higher prevalence than current study (Bowirrat *et al*., 2006).

The lower prevalence of depression based on MINI and GDS-15 in our study could be attributed to the small sample size and the design of study which is cross sectional study as the assessment of depression was only made one point of time which is only during the time of study period. This might not captured the patients who developed depression outside the study period hence lower the prevalence of the depression in this current study.

The study samples that were taken from psychogeriatric clinic and memory clinic in the tertiary and teaching hospital would also contributed to the difference and the lower prevalence in this study as compared with other study which was more of community based study.

The cases that were referred to the tertiary and teaching hospital usually were the more severe cases and this might not be able to be included in this study as those patients might not be able to comprehend and answer the questionnaires that also might contribute to the lower prevalence in this study.

Apart from that, most patients were recruited from UMMC which located in Petaling Jaya, an urban and affluent area with high socioeconomic status that contributes to lower prevalence of depression in patients with dementia in this study as suggested by many studies that depression is more common in lower socioeconomic status and rural area (Murata, Kondo, Hirai, Ichida & Ojima, 2008; Back & Lee, 2011; Hosseinpoor *et al*., 2012).

### 6.3 Associated socio-demographic and clinical factors with depression based on GDS-15

We analyzed GDS-15 as continuous data during the univariate analysis and after we found the significant factors, we further analyzed the GDS-15 as categorical data with cut-off 5 or more as depressed.

There were no difference between the median GDS-15 score for Malays and Non Malays; those married and those who were widowed, single or divorcee and the patients with or without employment history in our study. In terms of marital status, the finding was consistent with the study by Kales and colleagues (2005) which found that the patients with dementia with depression based on GDS were more prevalent in patients who were married compared with those who were not married.

In this study, the median GDS-15 score were higher in patient with age less than 75 years old compared with patients aged more than 75 years old in which younger patients score higher compared with older patient that was contradicted to the finding from Kales and team (2005).

The median score of GDS-15 of male patients in this study were the same when compared with the female patients. Study samples that were staying in nursing home had median scored of their GDS-15 which is higher compared with those staying with the family. There were no available data in the studies that used GDS to assess depression in patients with dementia as one study done in only male samples while the

other study did not mention about the gender distribution and patients were staying in nursing home.

Median score of GDS-15 in those patients with family income of more than RM 2000 were also higher compared with the patients with family income of less than RM 2000. Our study did not able to show any significant associations between patient's age, gender, having children and living status with GDS-15 score.

The only socio-demographic factor that found to be significantly associated with the GDS-15 score in our study is the educational status which patients with education level of primary school level or less had higher median GDS-15 score as compared with those who had educational level of secondary school and tertiary level of education with p value of 0.023. This finding is in keeping with finding of study by Lobo (1995) that suggested that increase in psychiatric morbidity with decrease in educational level.

In our study, the patients with dementia who did not have medical illness had median scored of their GDS-15 higher compared with those who had medical illness. This finding is contradicts with the study done by Kales and colleagues (2005). The median GDS-15 score were higher in patient with past psychiatry history compared with patients without past psychiatry history and also with the patients with other types of dementia as compared to the patients with Alzheimer's dementia, however there was no such study using GDS to diagnose depression that looking into this factors to compare with.

However, medical co-morbidity status, past psychiatry history and types of dementia were not found to be significantly associated with GDS-15 score in this study.

In this study, the clinical factors that found to be significantly associated with the GDS-15 score were prescription of antipsychotic and the severity of dementia based on MMSE score. Patients who were on antipsychotic had higher median GDS-15 score as compared with patients who were not on antipsychotic with p value of 0.047. This significant association is due to depression being part of behavioural and psychological symptoms of dementia (BPSD). Antipsychotic were prescribed to the patient with behavioural and psychological symptoms of dementia to control symptoms such as agitation, aggression and psychosis that could distress the care givers. Prado-Jean and colleagues found that most common additional symptoms of depression in patients with dementia were agitation, anxiety and irritability (Prado-Jean et al., 2010). As elderly people with depression present differently with agitation rather than the usual presentation in adult as suggested also by Hegeman (2012), depression might being missed in the group of patient with behavioural and psychological symptoms of dementia who was put on antipsychotics. Antipsychotic should be time limited and used on top of psychosocial intervention and the caregivers must involved with the plan of treatment (Clinical Practice Guidelines, 2009).

The median GDS-15 score for patients with moderate dementia were higher as compared with mild dementia patients with p value of 0.001. Logistic regression analysis showed that after adjustment for age, gender, marital status, level of education, living status, duration of diagnosis, dementia medication and antipsychotic prescription, severity of dementia were significantly associated with depression based on GDS-15 with cut-off 5 and above. The patients with moderate dementia is 6 times more likely to

have depression as compared to patients with mild dementia after adjusting for age, gender, marital status, level of education, living status, duration of diagnosis, dementia medication and antipsychotic prescription with p value of 0.006 (CI=1.661-20.747).

This finding that patients with moderate dementia were more likely to be depressed as compared to the patients with mild dementia was consistent with the suggestion of Forsell and colleagues (1993) that depression become more frequent as the disease progress from mild to moderate dementia. Our finding is also supported by the study by Mega, Cummings, Fiorello and Gornbein (1996) that as the dementia progress, the more prevalent the depression would be. Whereas Evers and colleagues (2002) and Lopez and colleagues (2003) reported that the depression is more prevalence in mild and moderate dementia as compared with severe dementia in their study samples.

There were studies with different finding of depression is more prevalence in patient with mild or early stage of dementia as compared with severe dementia (Lobo *et al*., 1995; Johnson *et al*., 2011). While a study by Lyketsos and team (1997) and a review by Verkaik and colleagues (2007) reported that there was lack of association between severity of dementia and the prevalence of depression.

### 6.4 Associated socio-demographic and clinical factors with depression based on M.I.N.I

From the univariate analysis of the socio-demographic and clinical variables with depression based on MINI, there were no variables that significantly associated with depression based on MINI. However, we will discuss more of proportion of those who

found to be depressed as compared with those who were not depressed and compare the figure with the other studies.

Based on MINI, proportion of patient that found to be depressed are more frequent in those aged younger compared with the older old with 12.5% diagnosed to have major depressive disorder in patients less than 75 years old as compared with 8.6% of those aged more than 75 years old were found to be depressed. This finding is in accordance with the study done by Blazer and colleagues that revealed that there were fewer depressive symptoms in oldest old as compare to young old when factor such as cognitive impairment was taken into account (Blazer, Burchett, Service & George, 1991). However, Steffens and his team (2009) found that the prevalence of depression was higher in older old group compared with young old group but not all subjects in their study were having dementia (Steffens, Fisher, Langa, Potter & Plassman, 2009). Our study also contradicted the result from study done by Castilla-Puentes and Habeych (2010) which revealed that depression was more prevalent in older old and this difference was due to much larger sample size and the different in methodology as the definition of depression in their study which was only by the diagnosis recorded in the database and not by using any specific questionnaire.

The proportions of male and female who were diagnose to have depression in current study were almost the same with 10.9% and 10.3% of male and female patients respectively. This finding is contradicted with other studies that found that the prevalence of depression is more in female as compared with male. A study by Verkaik and team (2009) showed that 80% of the patients with dementia and co-morbid depression were female. Bowirrat and colleagues (2006) found that 63 out of 99

depressed patients (63.6%) with Alzheimer's disease and 23 out of 42 depressed patients (54.8%) with vascular dementia were female but it was not found to be statistically significant. Same goes with the studies by Starkstein and colleagues (2005) and in the Zaragoza study of the elderly community in a Southern European Population by Lobo and team (1995) that have the same finding of proportion of female patient with dementia and co-morbid depression were higher compared with the male patients with dementia.

In this study, we found that 11.6% of the married sample had major depressive disorder while 8.9% of those who either widowed, single or divorcee had depression. This finding is not in accordance with other studies that showed that prevalence of depression is higher in widowed or single elderly. Dillon and colleagues revealed that marital status was significantly associated with depression in patients attending memory clinic with lower prevalence in subjects who is married (Dillon *et al*., 2011). In a study by Verkaik and his team (2009) found that about 70% of dementia patient with depression were widow or widower as compared with 24%, 4% and 2% were married, divorced or single respectively. The difference of the finding between our study and the other studies were due to the small number of sample in current study as compared with the other studies. Studies that were done in elderly population in Asia also showed that depression was more prevalent in widowed or not married (Chong *et al*, 2001; Murata *et al*., 2008).

Proportions of patients with dementia who were found to have depression among the patients that were staying in nursing home were higher with 27.3% compared with the proportion of depressed patient among those who were staying with the family which

was 8.7%. The proportion among the patients staying in nursing and found to be depressed was comparable with a study by Evers and colleagues (2002) that found 29% of dementia patient in chronic care facilities was diagnosed with major depression.

Our study also found that among the patients with education level of primary school or lower, 12.7% of them were depressed while proportion of depressed patient within the patients with education level of secondary school or higher was 8.5%. This study showed that higher proportion of depressed patient in patient with primary education or lower as compared with those with education level of secondary school or higher. This finding was in keeping with the Zaragoza study that revealed that higher prevalence of depression in dementia patient with lower level of education (Lobo *et al*., 1995). Bowirrat and team (2006) also found that proportion of depressed patients with no education were higher as compared with dementia patients with education background. However, study by Starkstein and colleagues (2005) did not find any difference between dementia patient with and without depression in term of their education level.

Among the patients with concurrent medical illness in this study, 10.2 % of them were diagnosed to have major depressive episode based on M.I.N.I. and this figure is lower as compared with the patients without the medical problems with 11.5%. Barca and her team found that physical disorder was more frequent in depressed patients with Alzheimer's disease but not with other type of dementia (Barca et al., 2012). The finding in our study was not in keeping with the study by Kaup and colleagues (2007) which revealed that group with the most co-morbidities was significantly associated with depression in patients with dementia when they further divide the group of those having medical problems according to number of medical co-morbidity . Our study was

also not consistent with the finding on a study on aged primary health care attendees in Greece found that diabetes mellitus and hypertension were the co-morbidities that frequently co-exist with depression and dementia (Argyriadou *et al*., 2001).

In this study, none of the patient who had history of psychiatric illness was diagnosed to have major depressive episode while 11.4% of those who did not have previous psychiatry history diagnosed to have major depressive episode. Study by Starkstein and team (2005) also found that personal history of affective disorder did not differ between patients diagnosed to have dementia with and without depression. However, this result was not in keeping with the study Barca and colleagues which showed that previous history of depression was significantly associated with the subjects with Alzheimer's disease (Barca *et al*., 2012). Ballard and team also found significant association between previous history of depression and current depression in their study samples with vascular dementia (Ballard *et al*., 2000). Previous depressive episode was also more prevalent in patient with current depression in a study done on patients with moderate Alzheimer's disease (Porta-Etessam *et al*., 2011).

Total of 15.4% of patient with moderate dementia in our study were found to have depression and this figure was higher as compared with depressed patients with mild dementia (4.1%) that showed that depression is more frequent in patients with moderate than in mild dementia. Dufoil, Fuhrer, Dartigues and Alperovitch (1996) had the similar finding of high level of depression was associated with higher cognitive impairment. The finding of our study was contradicted with the finding of other studies that showed depression is more prevalence in patient with mild or early stage of dementia as compared with severe dementia (Lobo, Pedro, Guillermo, Jose-Luis & Concepcion,

1995; Johnson, Watts, Chapin, Anderson & Burns, 2011). There were also studies that found lack of association of the severity of dementia and depression (Lyketsos *et al*., 1997; Verkaik *et al*., 2007).

However, in our study, we were unable to demonstrate any statistical significant associated socio-demographic and clinical factors with depression based on MINI due to small sample size as compared to other bigger sample size or in community setting.

### 6.5 Correlation of Geriatric Depression Scale 15 item (GDS-15) score with Mini Mental State Examination (MMSE) score

We were able to demonstrate the correlation between GDS-15 score and MMSE score that is negatively correlated with Pearson's Correlation Coefficient, r of -0.335 and p value of less than 0.01. This finding suggests that the lower the MMSE score in a patient, the higher would be his GDS score. This means that the more severe the dementia, the more depressed patient would be. This is consistent with the finding of the study by Dufouil, Fuhrer, Dartigues and Alperovitch (1996) that the severe the dementia, the level of depression would be increased.

### 6.6 Depressive symptoms based on Geriatric Depression Scale 15 items (GDS-15) between mild and moderate dementia

In our study, we found that there were three items that showed high number of patients scored 1 which were item 2, 9 and 10; which more than half of patients in this study had

dropped many of their activities, as they preferred to stay at home and thought that they have problem with memory.

Item 2 “Have you drop many of your activities and interest?”, item 6 “Are you afraid that something bad is going to happen to you?”, item 9 “Do you prefer to stay at home, rather than going out and do new things?”, item 10 “Do you feel you have problem with memory than most?” and item 13 “Do you feel full of energy?”; all of these items were found to be significantly scored 1 by patient with moderate dementia as compared to the patient with mild dementia. However, study by Teh and Hasanah (2004) found out that the Item 9 from the Malay version of GDS could not differentiate between cases and non-cases. This could be due to different sample and setting that being studies between our study and the study done by Teh and Hasanah (2004).

As a conclusion, it is very important to detect depression in patients with dementia as it is not uncommon in this group of patients. It can be detected by using tool such as GDS-15 which is simple and user friendly even in patients with dementia. Early detection of depression will lead to early intervention and therefore better quality of life for the patients and care givers and add better life in years for the elderly.

## 6.7 Strengths and limitations of this study

### 6.7.1 Strengths of this study

This study is the first study that we know of to look into the prevalence of depression in our local setting. Therefore this study could give a baseline data for further research in the same field.

The subjects in this study had been assessed and diagnosed to have dementia by trained and experienced geriatrician or psychiatrist after proper and thorough investigations done in each centres.

The other strength of this study is the instruments that were used were already translated into Malay and also had been validated in our local setting.

Our study have an adequate power of study as we managed to collect sample as per requirement by the calculation of sample suggest by Naing and colleagues (2006) and the power of our study was 80%. Apart from that, the other strength of this study is that all the study samples had completed all the questionnaires and the instruments and there were no missing data and all analyses were complete as well.

In this study, in term of statistical analyses, multivariate analysis was done which give stronger association to be observed in some of our variables as compared with only univariate study.

### 6.7.2 Limitations of this study

This study has certain limitations that should be considered when interpreting the result. Firstly, this study is a cross sectional study that only can demonstrate association but not cause and effect relationship of the variables and the outcome which is depression in patients with dementia.

The study samples were smaller as compared to other studies done within the same field even though the sample was sufficient when calculated based on the formula for prevalence study. The other limitation of this study as we are using convenient sampling is that only the patients who come on the specific day in the memory or psychogeriatric clinic were include into the samples but not all patients included as samples and this could lead to selection bias.

Apart from that, the study samples were recruited from tertiary hospital and teaching hospital therefore the findings of this study could not be entirely generalised to patients with dementia elsewhere. The generalisability of this study was also restricted by the exclusion of the dementia patients who could not understand Malay or English.

We did not diagnose the type of dementia using specific criteria such as NINDS-AIREN criteria or Lund and Manchester Criteria that might also result in bias. In this study, we only examine the duration of patient being diagnosed or presented to clinic that did not really represent the duration of illness from the onset of dementia way before the patients brought to treatment.

We used Geriatric Depression Scale 15 items to screen and M.I.N.I to diagnosed depression in the patients with dementia as it is more feasible for the elderly patients in busy clinic setting. However, the better and more accurate tool to diagnose depression specifically in the patients with dementia would be by using the Cornell Scale for Depression in Dementia, but due to the time constraint and no validation study done in our population; this scale was not being used in this study.

Another limitation in this study is that a small number of patients who could not read the GDS-15 needed help of the researcher to read the questionnaire for them which could also lead to bias.

This study only recruited patient with mild and moderate dementia and did not include patients with severe dementia which the result could not be generalized to all dementia patients.

# CHAPTER 7 CONCLUSIONS AND SUGGESTIONS

## 7.1 Conclusions

From our study, the prevalence of major depressive disorder in patients with dementia using M.I.N.I was 10.5 % and prevalence of depression based on GDS-15 with cut-off 5 or more was 20.2%.

We also found that the severity of dementia was significantly associated with depression based on GDS-15. The patients with moderate dementia are 6 times more likely to have depression as compared to patients with mild dementia.

Apart from that, the MMSE score was negatively correlated with GDS-15 score which is the more severe the dementia the more depressed the patient would be.

At least 1 in 10 patients with dementia have depression hence it is important to screen early for depression at all stages followed by early intervention so that the patients would get proper treatment and quality of life thus adds life to their years.

## 7.2 Suggestions

The study would be better if it is done in a multi-centre setting including the rural area and other states or study in community setting that would enable the result to be generalized to the rest of Malaysian population.

The usage of more specific criteria to diagnose type of dementia and the usage of Cornell Scale for Depression in Dementia would diagnose depression in specifically for dementia patients, however, the scale need to be validated first in our population.

The use of Montreal Cognitive Assessment (MOCA) is also another option to assess patients' cognitive function as (MOCA) also has Malay version and is readily available in public domain. However, MOCA is not validated for assessment of severity of dementia. The better tools to assess severity of dementia are the Clinical Dementia Rating Scale (CDR) or Global Deterioration Scale (GDS).

Apart from that, future study can also be done to look into social support and patient's functionality which also associated with depression in the elderly which is not done in this current study.

The general practitioner, primary care doctors and memory clinic doctors can use GDS-15 to detect depression in patients with dementia. In the centre with geriatric or psychogeriatric specialty, the doctor in memory clinic themselves can treat the patients

with dementia who are depressed. Whereas, the centre without geriatric specialty, the patient with GDS-15 score of 5 or more can be referred to the psychogeriatrician or psychiatric unit for further assessment and management.

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