

VOLUME 2

• ISSUE 1 •

DECEMBER 2015



# MANIPAL ALUMNI SCIENCE AND HEALTH JOURNAL

**MANIPAL ALUMNI ASSOCIATION MALAYSIA**

7A, Jalan Telawi Lima 59100 Bangsar Baru  
Kuala Lumpur, Malaysia  
Phone: +603-2282 7355 Fax: +603-2282 8355  
Email: manipalghsc@gmail.com / manipalmaam@gmail.com  
www.manipal.org.my]

# Editorial Board

---

## Editor-in-Chief

Dr. Prem Kumar Chandrasekaran (Malaysia)

## Sub-editors

Review Articles  
Original Articles  
Case Reports  
Medical Students'  
Anecdote Section

Associate Professor Dr. Philip George (Malaysia)  
Dr. Sivakumar Thurairajasingam (Malaysia)  
Dr. Sanjay Woodhull (Malaysia)  
Professor Dr. Jaspal Singh Sahota (Malaysia)

## Section Editors

Anaesthesia  
Dentistry  
ENT  
Family Medicine  
General Surgery  
Internal Medicine  
Obstetrics & Gynaecology  
Oncology  
Ophthalmology  
Orthopaedics  
Paediatrics  
Psychological Medicine  
Radiology

Dr. Sham Kumar Sadanand (Malaysia)  
Dr. Jeyalan Samanther (Malaysia)  
Dr Balachandran Appoo (Malaysia)  
Associate Professor Dr. Jayakumar Gurusamy (Malaysia)  
Dr. Patricia Gomez (Malaysia)  
Datuk Dr. N. Arumugam (Malaysia)  
Dr. Selvaganesan Sockalingam (Malaysia)  
Dr. Jayendran Dharmaratnam (Malaysia)  
Dr. Francesca Martina Vendargon (Malaysia)  
Dato Dr. Selvakumar Kanagarajah (Malaysia)  
Dr. Akila Venkataraman (USA)  
Dr. Dr. Nagesh Pai (Australia)  
Dr. Vijayalakshmi Krishnapillai (Malaysia)

## Members of Peer-review Committee:

Dr. Vanitha Sivanaser	Malaysia
Dr. Vazeer Ahmed	UK
Dr. Vijayavel Vadiveloo	Malaysia
Dr. Bhaskaran Gobalakrishnan	Malaysia
Associate Professor Dr. Sushil Kumar Vasudevan	Malaysia
Dr. Josephine Subramaniam	Malaysia
Dr. Harichandran Thambyrajah	Malaysia
Dr. Mahadev Shunmugam	Malaysia
Dr. Riza Ibrahim	UK
Dr. Mohamed Nazir	Malaysia
Dr. Oh Kim Soon	Malaysia
Dr. Manohar Pathmanathan	Malaysia
Dr. Surinder Singh	Malaysia

## Advisory Board

### Regional

Dr. Rajbans Singh	Malaysia
Dr. Muruga Vadivel	Singapore
Datuk Dr. Devan Pillai	Malaysia
Dr. Suresh Kumarasamy	Malaysia
Professor Dr. Premnath Nagalingam	Malaysia

### International

Dr. R.C. Krishna	USA
Dr. Unni Krishnan Karunakara	USA
Dr. Rajiv Nanda	USA
Professor Dr. Lucy Gilbert	Canada

### Peer-review Process

All submitted articles will first be screened by the Editorial Board to see if the articles confirm to the standard and style of the journal as per the manuscript submission criteria. The article is then sent to a member of the Peer Review Committee for scrutinising and feedback before being accepted for publication.

## **EDITORIAL NOTE**

---

Dear Colleagues of MAAM,

As we close the year for 2015, we continue to be thankful for being given the chance to be part of the caring process in the health delivery system; at the same time, we are also mindful of the obstacles we have in our path to improved healthcare. As we reflect on the health issues that have plagued the globe this year, we need to be well-informed and employ evidence-based findings that are constantly evolving.

We at the Editorial Board of the MASH Journal have also been doing our own reflection on its significance and our target audience, and thence its contributors. With the increasing focus on impact factors in publications, we are aware that career promotions of those in the academia would depend on securing higher points in universally recognised research awarding systems. Hence, we re-iterate that the main focus of the Journal is to encourage a research-based mindset among our future doctors and since they will be the ones eventually taking over the medical and dental landscape (and our care in the twilight years), that is good enough reason for us all to be more involved in nurturing and guiding them. Of course, no one is duty-bound to contribute as we are well aware that everybody has become busier nowadays but we would like to instead emphasise that any help in aiding this Journal to pick up speed in its infancy would be most welcome. We requested write-ups from experts in various fields but have received none to date. Nevertheless, we understand that more time is required to build up the Alumni's confidence in the viability of this endeavour and therefore, had to resort to consider putting up personal studies some of us had pending so as to gather sufficient material to produce an Issue. We were also delighted by a contribution from a member currently completing specialty training. We also felt previously unpublished papers, if made more simple for the undergraduate level, were appropriate and hope that would in turn encourage submissions from the medical students of MMMC themselves – that would then satisfy the primary purpose of this Journal. Therefore, considering the rather dismal response, the Board has decided that we would have only one Volume/Issue this year.

As the Journal is in the process of being assigned an ISSN number by the National Library of Malaysia, for the sake of professionalism, it will be known by its full title “Manipal Alumni Science and Health Journal” insofar as the medical world is concerned once that listing is secured; nevertheless, we can still retain the popularly abbreviated “MASH Journal” in parlance amongst ourselves. However, getting the Journal indexed will be a long process and for that, we cannot rely purely on undergraduate contributions. Thus, we will need more proactive intervention next year to keep this Journal relevant to the medical community. But for now, we are starting small and this Issue will showcase two very simple Original studies that have been done before with no external funding and our point is that research can be done by anyone, provided the correct principles are applied and the eventual message thereof succinctly delivered. A Review article not previously published

was also extracted from a medical newsletter and formatted to our accepted scientific guidelines. And lastly, an interesting Case study is also hereby presented – due to the coincidental specialties of the present contributors, we have had no choice but to focus this Issue towards psychiatry, neuropsychiatry and neurology. With more contributions from other fields in future, we are confident subsequent Volumes will be able to focus on various other specialties and we look forward to submissions from all of you to keep up the good name of our ever active MAAM. Finally, a big appreciation goes out to our reviewers who selflessly offered their time in providing their valuable comments and opinions on the various articles accepted in this Issue of the MASH Journal.

We hope you enjoy this 2<sup>nd</sup> Volume and best wishes to everyone for 2016 from all of us in the Editorial team.

Prem Kumar Chandrasekaran  
Editor, on behalf of the MASH Journal Editorial Board

**REVIEW ARTICLE****The Pseudodementia Dilemma**PK Chandrasekaran<sup>1</sup>, VR Russell<sup>2</sup>

*Corresponding Author : Dr. Prem Kumar Chandrasekaran, Consultant Neuropsychiatrist, Penang Adventist Hospital, 465 Burmah Road, 10350 Penang, Malaysia. E-mail: [premkumar@pah.com.my](mailto:premkumar@pah.com.my)*

**Key words:** Pseudodementia, dementia, Alzheimer's disease, vascular, depression

**Introduction**

Pseudodementia refers to a condition resembling organic dementia to which underlying physical disease makes little or no contribution. It describes a clinical picture characterised by a reversible dementia syndrome secondary to a primary psychiatric disorder. The concept has proved to be popular clinically although it is not classified as a diagnosis in either DSM-V or ICD-10. Pseudodementia is clearly not a single nosological entity as was once thought but rather a syndrome of relative clinical consistency, reflecting multiple and diverse underlying psychiatric aetiologies.

Since its origins in the 19<sup>th</sup> century, research interest in it has waxed and waned and opinions about its clinical utility have been divided. Following the revival of the term 'pseudodementia' in the 1960s,<sup>1</sup> there have been further controversies surrounding its use of the term, ranging from affirmations that it is a distinct entity to speculations that it represents a harbinger of dementia. It has frequently been dismissed as redundant while some experts have urged its abandonment altogether. On the other hand, some researchers had endeavoured to validate the clinical utility of the term 'pseudodementia' and met with success.

It is interesting to retrospectively examine how ideas related to initial observations have carved a path towards our current understanding and approach to this condition. In this article, we will elaborate mainly on the commonest manifestation – depressive pseudodementia. Despite many advances in the fast-developing field of neuropsychiatry, countless errors and post-hoc changes makes this subtype worthy of special consideration. However, we shall not neglect the impact of the other phenomena that have also been

<sup>1</sup> Neurobehavioural Medicine, Penang Adventist Hospital

<sup>2</sup> Department of Psychiatry, Penang Medical College.

described under the broad heading of pseudodementia, namely hysterical pseudodementia, Ganser's syndrome and simulated dementia.<sup>2</sup> Finally, differentiating this condition from bipolar illness and schizophrenia is also worthy of mention.

### **1. *Depressive Pseudodementia (DPD)***

Some patients with depression do not exhibit hallmark symptoms of depression. Some signs and symptoms like psychomotor retardation, anhedonia, laboured thinking, slipshod behavior, failing to register events, faulty orientation and loss of recent memory should alert clinician to possibility of this category of pseudodementia. The 1961 publication by Kiloh entitled "Pseudo-dementia" revived this concept from a previously obscure and ambiguous position somewhere between hysteria and malingering.<sup>1</sup> He described the above set of symptoms with additionally self-neglect and loss of weight while Post (1965) added those symptoms to observations of tremulous elderly patients with shuffling gait. Kiloh urged that the possibility of depression be considered before diagnosing all cases of dementia and his paper had a major impact, leading to a surge of interest in what came to be referred to as DPD in the period between the 1960s and 1980s. Several more follow-up studies supported his argument for examining all patients for potentially reversible causes of apparent dementia.

Nevertheless, Folstein & McHugh (1978) claimed both dementia and depression interact together and that the term 'pseudodementia' was a misnomer as cognitive deficits resolve when the depression resolves. Thus they suggested the term 'dementia syndrome of depression'.<sup>3</sup> This brings us to the question, "Could depression then be a reaction to cognitive impairment in dementia?" Reifler et al (1982) felt that was so but only in mild and early cases of dementia.<sup>4</sup> By the 1980s, doubts were being cast upon the claimed reversibility of pseudodementia, based on longer follow-up periods in outcome studies. Several subsequent studies found that if followed for long enough periods, many patients whose cognitive deficits had initially appeared to have been reversed by psychiatric treatments went on to fulfill diagnostic criteria for dementia. A more recent meta-analysis carried out by Ownby et al (2006) found that depression was associated with a doubling of the risk for subsequent dementia.<sup>5</sup> Finally, Korczyn & Halperin (2009) rationalized that since depression and dementia are both common in old age and frequently occur together, white matter changes both in Alzheimer's Disease (AD) and in depression result from vascular changes, supporting the concept of 'vascular depression'.

Rabins et al (1984) found that treatment of depression improved MMSE scores with a rise to normal scores two years later in their 'depressed/demented' group. Post (1965) and Burgeois et al (1970) found that Electroconvulsive therapy (ECT) was especially effective in this group, a consistent finding most recently echoed by Rapinesi et al (2013).<sup>6</sup> In an article commemorating the 50<sup>th</sup> anniversary of Kiloh's classic paper, Snowden (2011) points out that the concept of pseudodementia may be worth retaining even insofar as the cognitive deficits in depressive pseudodementia may be at least temporally reversed and true dementia postponed as a result of active treatment.<sup>7</sup> Hence, we thought it appropriate



to include Small et al's (1981) proposed features to differentiate dementia from DPD (Table 1).

## **2. *Ganser's Syndrome***

This was first described by Ganser in 1897. Frequently, the focus is on the classic symptoms of '*vorbeireden*' or approximate answers or answering past the point, which Scott (1965) described as Ganser's symptom and which is commoner than the syndrome itself. However, this has led to other features being overlooked, for example prominent hallucinatory experiences (pseudohallucinations), hysterical stigmata and fluctuating disturbance in consciousness. Resolution is abrupt with complete and sometimes, residual amnesia ('hysterical twilight state') for the brief duration of the illness, which Ganser (1898) himself believed was central to the presentation.<sup>2</sup>

The apparent dementia that accompanies approximate answers in Ganser's syndrome is usually incomplete, inconsistent and self-contradictory. These patients are able to adapt to demands of daily life which those with organic dementia cannot. Motor behavior ranges from dazed stupor to histrionic outbursts of excitement. Mood ranges from apathetic indifference to anxious bewilderment. Whitlock (1967) called it the 'buffonery syndrome of schizophrenia' from the associated confabulation and childish, playful attitude. The change in consciousness, as well as the conversion symptoms, was proof that this is a hysterical syndrome and not just simple malingering. Thus it has been grouped under dissociative disorders in the DSM-V and under other dissociative (conversion) disorders in ICD-10.

Ganser's syndrome can occur during the course of a depressive illness, head injury, early dementia, alcoholism and other toxic states and purely as a response to emotional trauma. It is felt that organic and psychogenic factors operate together here. The concept of gain had led to the term 'prison psychosis' and although malingering can be suspected, of note is that patients do not provide spontaneous absurd remarks, merely answers to questions they were asked.

## **3. *Hysterical Pseudodementia***

Mechanisms of hysterical dissociation may operate to some degree in pseudodementia. Conversion pseudodementia in older people is felt to be caused by a catastrophic reaction to cumulative loss in later life in individuals with predisposing borderline and narcissistic traits. Hepple (2004), reminiscing Wernicke's 1906 original conceptualization, refocused attention on the possible psychological basis on patients with pseudodementia. He contended that the syndrome is more common in women from a higher socio-economic background with past psychiatric histories dominated by depressive symptoms.

The core features are apparent cognitive impairment, regression and increasing physical dependency. Other symptoms could include the classical sensory loss, paralysis and 'belle indifference' of conversion.<sup>2</sup> There can be fatuous cheerfulness or sullen apathy and in severe cases, hysterical puerilism, infantilism and amnesia. There appeared to be no



response, in Hepple's case series, to various treatments for depression. The prognosis was considered poor.

Treatment using psychotherapeutic approaches may limit the progression of the syndrome if recognised at an early stage. The role of abreaction and sleep deprivation was described by Patrick & Hommels (1990), who conversely found that confusion was exacerbated with those modalities in patients having organic dementia.

#### **4. *Simulated Dementia***

In this subtype, memory loss appears to be an isolated main symptom.<sup>2</sup> There could also be mutism and lack of cooperation. Anderson et al (1989) found that it was not possible to convincingly feign dementia – with repeated efforts, fatigue sets in and a 'pull on reality' would be experienced.

Hunt (1973) used the MMPI to distinguish a malingerer from one with organic dementia as the series of questions were designed to weed out inconsistencies and a malingerer would get anxious and upset when slips were pointed out, as observed by Kraupl-Taylor (1966). A point in differentiating those simulating dementia is that they would appear to be more 'superficial' than patients with Ganser's syndrome. There will be an increase in conscious malingering and the course of the disorder is longer and relapsing. There will also be an absence of melancholia present in DPD.

#### **Other Considerations**

Sometimes, functional disorders have dementia-like symptoms and in hypomania, distractibility and random answers can mimic disorientation and failing memory; playfulness could lead to false replies. Carney (1983) observed that manic overactivity can be mistaken for agitation. In schizophrenia, poverty of ideas, emotional blunting and an unkempt state may suggest dementia. Confusing the clinical picture is the presence of late paraphrenia (Roth, 1981) and demonstration of the presence of mild cognitive disorder and enlargement of ventricles (Naquib & Levy, 1987).

#### **Final remarks**

Pseudodementia would seem to represent a term which is impossible to adopt uncritically but which equally should not be discarded completely as a potentially useful theoretical and clinical construct. The likelihood is that it will continue to pose a dilemma to present day clinicians, researchers and medical educators.

Notwithstanding the considerable evidence that most patients with pseudodementia have a latent tendency to progress to dementia, our own conclusions are that there is merit in retaining the concept as a descriptive term, particularly in relation to the phenomenon of depressive pseudodementia.

Depression remains as a common, treatable condition that is all too often underdiagnosed and untreated. This is more likely when it presents with co-morbid medical conditions in older patients. Recent studies have drawn attention to the fact that depression may be inappropriately labeled as 'understandable' in such patients – both by patients and clinicians. The reality is that most older people, even those with major medical co-morbidity, are not clinically depressed and when they are, depression should never be ignored as they do require and respond to treatment. If we add the cognitive impairment to the clinical picture in these patients, it increases the risk of 'normalising' their depressive symptoms and missing treatment opportunities that could greatly improve the medical outcome and quality of life.

### Source

1. Kiloh LG. Pseudo-dementia. Acta Psychiatrica Scandinavia 1961; 37; 336-51.
2. Lishman WA: Organic psychiatry - the psychological consequences of cerebral disorder (3<sup>rd</sup> edition). Blackwell Science, 1998.
3. Folstein, M. F., & McHugh, P. R. (1978). Dementia syndrome of depression. In R. Katzman, R. Terry & K. Brick (Eds.), Alzheimer's disease: Senile dementia and related disorders. New York Raven Press.
4. Reifier, B. V., Larson, E., Hanley, R. (1982). Coexistence of cognitive impairment and depression in geriatric outpatients. American Journal of Psychiatry, X39,623-626.
5. Ownby RL et al. Depression and risk of alzheimer's disease: systematic review, meta-analysis and meta-regression analysis. Archives of General Psychiatry 2006, 63: 530-8.
6. Rapinesi et al. Depressive pseudodementia in the elderly: effectiveness of electroconvulsive therapy. International Journal of Geriatric Psychiatry 2013; 28: 433-40.
7. Snowden J. Pseudodementia, a term for its time: the impact of Leslie Kiloh's 1961 paper. Australasian Psychiatry 2011; 0: 391-7.

***(This article was published in the Academy of Medicine of Malaysia (AMM) newsletter 'The Internist', August 2013 Issue and modified to conform to accepted scientific publication formatting)***

**Table 1 Differentiating Dementia from Depressive Pseudodementia**

<b>Characteristics</b>	<b>Dementia</b>	<b>DPD</b>
<b><i>History</i></b>		
Precise Onset	Unusual	Usual
Duration of symptoms	Long	Short
Rapid symptom progression	Unusual	Usual
Complaints of cognitive loss	Variable (minimized in later stages)	Emphasised
Description of cognitive loss	Vague	Detailed
Family awareness of dysfunction and severity	Variable (usual in later stages)	Usual
Loss of social skills	Late	Early
Psychopathology history	Uncommon	Common
<b><i>Examination</i></b>		
Memory loss for recent vs. remote events	Greater	About equal
Specific memory loss ('patchy' deficits)	Uncommon	Common
Attention and concentration	Often poor	Often good
'Don't know' answers	Uncommon	Common
'Near miss' answers	Variable (common in later stages)	Uncommon
Performance on tasks of similar difficulty	Consistent	Variable
Emotional reaction to symptoms	Variable (unconcerned/shallow in later stages)	Great distress
Affect	Labile, blunted or depressed	Depressed
Efforts in task performance	Great	Small
Efforts to cope with dysfunction	Maximal	Minimal

**ORIGINAL PAPER**

# Translation and Reliability of the Malay Version of the NUCOG – a Trial-run Study

PK Chandrasekaran <sup>1</sup>, PP George<sup>2</sup>, MA Walterfang<sup>3</sup>, D Velakoulis<sup>3</sup>

---

*Corresponding author: Dr. Prem Kumar Chandrasekaran, Consultant Neuropsychiatrist, Penang Adventist Hospital, 465 Burmah Road, George Town, 10350 Penang, Malaysia. Tel: 04-2227772. E-mail: [premkumar@pah.com.my](mailto:premkumar@pah.com.my)*

**Key words:** Cognitive impairment, visuo-constructional skills, declarative memory, executive functioning, reliability

## Abstract

**Objective:** The need for a comprehensive assessment tool in Bahasa Malaysia (Malay language) to detect cognitive impairment is rising. Further structured testing of the various aspects of cognition, the ease of administration, feasibility of time to administer the test and its applicability to both outpatients and inpatients were considered. Based on the above demands, the Neuropsychiatry Unit Cognitive Screening Instrument (NUCOG) was selected for translation and validation into the Malay language.

**Method:** It was first translated to Malay, then back-translated to English until changes made were comparable to the original English version (Phase 1). The Malay version was tested for Inter Rater Reliability (IRR) by Intra-class Correlation Co-efficient (ICC) and acceptability (Phase 2).

**Results:** The Malay version of the NUCOG proved reliable (**>0.97**). Matching it against the Malay version of the Mini-Mental State Examination (MMSE) for Construct Validity (Phase 3) will then validate it.

**Conclusion:** This Malay version is a time-efficient and reliable cognitive assessment tool that is expected to be of benefit to neuropsychiatric patients; however, further research with a larger sample is required to determine its validity in a Malay-speaking population.

---

<sup>1</sup> NeuroBehavioural Medicine, Penang Adventist Hospital, Penang

<sup>2</sup> Department of Psychiatry, International Medical University, Seremban

<sup>3</sup> Neuropsychiatry Unit, Royal Melbourne Hospital, Australia

## Introduction

The rate of medico-legal cases involving head injuries has risen and therefore, the need for a comprehensive assessment instrument in Bahasa Malaysia (Malay language) to detect cognitive impairment is increasing and demands that it should be applicable to an outpatient, as well as inpatient, setting. This must also take into account the ease of administration by any medically qualified professional and the feasible duration of time taken to administer it as exorbitant amounts of time are required for formal (and diagnostic) neuropsychological testing. The gold standard Mini Mental State Examination (MMSE), which takes about 7 minutes to administer, has been found to be unsuitable in some areas pertaining to our language and culture and even after the validation of its Malay version, it was still found to be non-encompassing and lacking detail into testing visuo-constructional skills, non-verbal and long-term declarative memory. Furthermore, impairment of executive cognitive functioning may not be clearly evident if the dysfunction is severe as MMSE scores may be normal while severe functional limitations may exist.<sup>1</sup> The Clock Drawing Test (CDT), which can better detect executive cognitive dysfunction, and the Elderly Cognitive Assessment Questionnaire (ECAQ), better suited for populations with lower literacy, are more time-efficient but serve more as primary screening tools for cognitive dysfunction. The validity of the ECAQ in a different language and culture has also yet to be examined.<sup>2</sup> The recently developed 10-minute Montreal Cognitive Assessment test (MoCA) is most effective in detecting Minimal Cognitive Impairment (MCI) and has been considered the only screening tool available to distinguish between persons who have MCI and those considered 'normal' but its sensitivity is greater in only mildly cognitive-impaired subjects.<sup>3</sup> The 'WORLD' test has rather high sensitivity and specificity,<sup>4</sup> and the Mini-Cog test, which takes only under a couple of minutes to administer but has been criticized for having limited sensitivity and specificity,<sup>5</sup> are too simple to be used in legal settings. So too is the 1-minute naming test on its own, which interestingly detects a particular dementia (i.e. of vascular origin) if words with the letter 'F' are less ably generated by a subject<sup>6</sup> – fortunately, this test is already incorporated into the novel cognitive assessment scale tested and the framework employed in this study, as are the CDT and Mini-Cog test but in mildly variable proportions.

The Neuropsychiatry Unit Cognitive Screening Instrument (NUCOG) compensates for those limitations and demonstrates a very strong correlation with the MMSE scores ( $r^2 = 0.78$ )<sup>7</sup> and thus, could possibly be used especially in from a medico-legal cases. It takes about 20 minutes to administer and is well-structured into five main areas testing attention, visuo-constructional skills, memory, executive cognitive functioning and language. Within these domains, there are further specific sub-scales totalling 25 with an add-on scoring system which when summed, gives a maximum score of 100.

We aimed to test the Inter Rater Reliability (IRR) of the Malay NUCOG between two raters after translating the scale into Malay, followed by back-translation to ensure maximal comparability to its original English version.

## Methods

### **Phase 1:**

The cognitive screening instrument was first translated into Malay by a bi-lingual psychiatrist. Thereafter, the translated version was back-translated into English by another bi-lingual psychiatrist who had not seen the actual English version. Modifications of mild discrepancies were made until the revised back-translated version was comparable to the original English version. However, only verbal commands to the patient were translated as it was expected that the medically-trained individual administering the test should be proficient in both languages. Further changes were made to adhere to the validated Malay version of the MMSE<sup>8</sup> as a number of items in the MMSE were already present in the NUCOG. Further tasks that involved culturally unacceptable aspects were also modified within limits.

### **Phase 2:**

Patients and controls from Penang Adventist Hospital and Seremban General Hospital were recruited. Prior to that, the Ethics Committee reviewed the study plan and considered it low-harm to subjects. The two raters then assessed 10 subjects separately by administering the Malay version of the NUCOG. The scores from each rater were determined and entered into an SPSS template. Each set was tested for IRR, that was measured by Intra-class Correlation Coefficient (ICC), as used in another Asian translation and validity study,<sup>9</sup> for total NUCOG and sub-scale scores by two-way and absolute agreement.

### **Phase 3:**

The NUCOG will be administered to patients with organicity over an indefinite period. The inclusion criterion is that all patients must fulfil a Diagnostic and Statistical Manual of Mental Disorders – 4<sup>th</sup> Edition (DSM-4) coding for a neuropsychiatric disorder(s). An Analysis of Variance (ANOVA), and controlling for age, will be done to compare the total NUCOG scores between the control and patient groups. Cognitive profiles across domains via a repeated measures model (and correcting for repeated measures using the Huynh-Feldt method) will be examined for significant of effect of group and significance of group by slice interaction. The crucial form of validation would be the Pearson correlation coefficient value when examining the relationship between the NUCOG and MMSE scores. Finally, the internal consistency of the tool across the whole sample will be re-examined as another form of reliability analysis using alpha studies.

## Results

The Phase 2 results are described here. The demographic data in this study found five females and one male in the control group and in the patient group, three males and one female. The mean age of controls was 35.5 yrs and that of patients 62.5 yrs. The mean years of education was 15.75 years in controls and 8.75 years in patients. The NUCOG was found to be time-efficient (Table 1), taking between 20-25 minutes (mean of 21.16 minutes in

controls and 28.0 minutes in patients) to administer to most subjects (including the 1 with MCI) by the two raters. However, the subjects with dysphasia, motoric dysfunction and depression required more time (35 minutes for rater 1 and between 32-38 minutes for rater 2, for the subjects with Vascular Dementia (VasD) and Alzheimer's Disease (AlzD) respectively). It was also interesting to note how closely both raters had rated the subjects, given the larger margin of scoring divisions for error (Figure 1). Statistical analyses proved this with a good IRR rating and acceptability was awarded for total NUCOG and subscale scores ( $>0.97$ ).

Given previous research involving the NUCOG, we expect a good correlation between the Malay NUCOG and Malay MMSE scores in Phase 3 (***results of this was published as a separate study: PK Chandrasekaran, MA Walterfang, D Velakoulis. Preliminary Data on the Validity Reliability of the Malay version of the NUCOG. Asian Journal of Psychiatry Dec 2010; 3(4): 186-189.***

## Discussion

For Phase 2, we chose more controls because the main study sample to test the properties of the instrument should be 'normal healthy subjects'. Those with dementia were easier for the researchers to recruit taking into consideration practical issues. Cronbach's alpha was selected for item analysis because the larger the numbers of items added together in a scale, the less the random error matters as it will be self-cancelling, therefore some reliability coefficients (such as Cronbach's alpha) also compute higher reliability when the number of scale items is higher. This rationale has been similarly used with success in other similar translation-reliability-validity studies.<sup>8,10,11</sup> Kappa co-efficient studies have been employed as 1<sup>st</sup> line analysis<sup>12</sup> but considering the higher number of items to be analyzed, we decided to go with the former for reasons mentioned above. With our data thus far, and given its apparent high reliability, it seems promising that the Malay NUCOG may also be a valid tool for assessing cognitive dysfunction given its strong correlation with the MMSE scores (Walterfang et al, 2006).<sup>7</sup>

The NUCOG is a much needed tool in our litigation-nervous medical atmosphere because it provides a more intrinsic picture of a person's cognitive state, whilst remaining time-efficient. It may be of benefit in medico-legal brain injury cases where comments on prognosis in terms of executive functioning and Activities of Daily Living (ADL) are expected. Furthermore, dementing illnesses can be earlier detected at their mild stages. We also feel the NUCOG may be applicable to substance-related disorders and this is currently under consideration for another study and it is hoped to be a valid and reliable tool to that end.



## Limitations

Firstly, the translation and back-translation process was rather simple and subjecting our version of the Malay NUCOG through the scrutiny of a panel of linguistic experts would have been more stringent. Next, we feel that the NUGOG may be unsuitable for those in the low literacy group. This was evidenced by lower scores in the respective specific subscales for those with less number of education years. Adding to that, although well-tolerated in adults, the NUCOG may possibly be unsuitable for non-adults and pre-secondary schoolers. Fourthly, we encountered time difficulties in those who had dysgraphia, motoric problems and depression. Also, the statistical analyses we employed were fairly basic and incorporating more modalities with test-retest reliability may further strengthen the results. Finally, recruiting suitable patients was problematic and our preliminary study sample number was small, indicating that further research with larger samples is clearly needed for a more accurate picture, especially within the specific subscales.

## Conclusions

The NUCOG is a more comprehensive assessment instrument for cognitive dysfunction because it compensates for limitations in testing into further detail visuoconstructional, non-verbal, long-term declarative memory and executive functioning skills lacking in other simpler but more time-efficient assessment tools. It is a reliable tool and is expected to be beneficial in neuropsychiatric patients, especially in the medico-legal arena and more especially when neuropsychological assessment is unavailable. However, further research needs to be done to get a more intrinsic picture of the exact value of the translated version of this novel cognitive screening instrument as its validity in a Malay-speaking population needs to be determined with a larger sample.

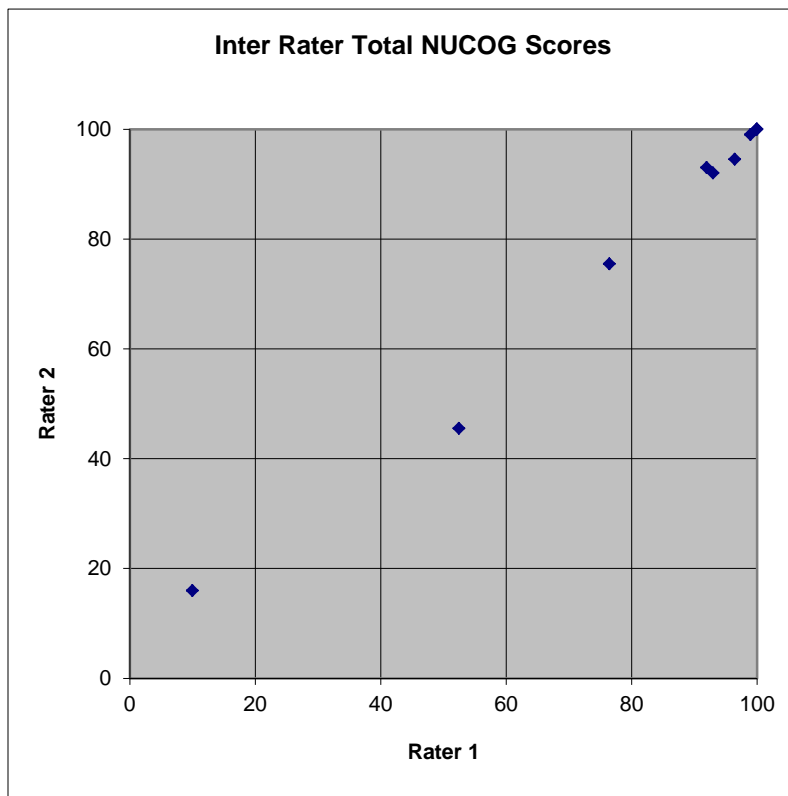
## References

1. Juby A, Tench S, Baker V. The value of clock drawing in identifying executive cognitive dysfunction in people with normal mini mental state examination score. *Canadian Med Ass J* 2002; 167(8): 859-64.
2. Kua EH, Ko SM. A questionnaire to screen for cognitive impairment among elderly people in developing countries. *Acta Psychiatr Scand* 1992; 85(2): 119-22.
3. Nasreddine ZS, Philips NA, Be'dirian V, et al. The Montreal cognitive assessment, MoCa: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 2005; 53: 695-9.
4. Leopold NA, Borson AJ. An alphabetical "world": a new version of an old test. *Neurol* 1997; 49: 1521-4.
5. Solomon PR, Hirschhoff A, Kelly B, et al. A 7-minute neurocognitive screening battery highly sensitive to alzheimer's disease. *Arch Neurol* 1998; 55: 349-55.

6. Duff Canning SJ, Leach L, Stuss D, et al. Diagnostic utility of abbreviated fluency measures in alzheimer's disease and vascular dementia. *Neurol* 2004; 62: 556-62.
7. Walterfang M, Siu R, Velakoulis D. The NUCOG: validity and reliability of a brief cognitive screening tool in neuropsychiatric patients. *Aust NZ J Psychiatry* 2006; 40(11-12): 995-1002.
8. Zarina ZA, Zahiruddin O, Che Wan AH. Validation of Malay mini mental state examination. *Malaysian J Psychiatry* March 2007; 16(1): 16-9.
9. Chan TSF, Lam LCW, Chin HFK. Validation of the Chinese version of the Zarit burden interview. *Hong Kong J Psychiatry* 2005; 15: 9-13.
10. Fountoulakis KN, Papadopoulou M, Kleanthous S, et al. Reliability and psychometric properties of the Greek translation of the state-trait anxiety inventory form Y: preliminary data. *Annals Gen Psychiatry* 2006; 5: 2.
11. Azhar MZ, Norma YIR, Noorjan KON. The Malay version of eating disorder belief questionnaire: preliminary development. *Malaysian J Psychiatry* September 2001; 9(2): 21-8.
12. Kochlar PH, Rajadhyaksha SS, Suvarna VR. Translation and validation of brief patient health questionnaire against DSM-IV depressive disorder in Indian patients. *J Postgraduate Medicine* 2007; 53(2): 102-7.

**Table 1 Demographic and Inter Rater Data**

n	Age	Sex	Education (years)	Diagnosis	Rater 1 Time (mins)	Rater 1 NUCOG score	Rater 2 Time (mins)	Rater 2 NUCOG score
1	68	M	6	1) VasD 2) Depression	35	52.5	32	45.5
2	72	M	5	MCI	20	76.5	20	75.5
3	68	M	13	1) AlzD 2) Nominal aphasia	35	10	38	16
4	38	F	11	Control (Inebriated)	22	93	24	92
5	61	F	14 ½	Control (Nurse)	25	96.5	24	94.5
6	61	F	11	Control (Nurse)	22	92	23	93
7	23	F	18	Control (Medical student)	20	100	20	100
8	23	M	17	Control (Medical student)	20	99	20	99
9	23	F	17	Control (Medical student)	20	100	20	100
10	22	F	17	Control (Medical student)	20	100	20	100

**Figure 1 Inter Rater Reliability**

**ORIGINAL PAPER**

**An Assessment of the Knowledge of Depression Amongst Students and Their Teachers in Seremban and Kuala Lumpur,**

PP George<sup>1</sup>, CM Chang<sup>2</sup>, ZK Chee<sup>2</sup>, CL Saw<sup>2</sup>, WJ Sow<sup>2</sup>

---

*Corresponding author: Associate Professor Dr. Philip George, Assistant Dean and Consultant Psychiatrist, International Medical University Clinical School, Jalan Rasah, Seremban, 70300 Negeri Sembilan, Malaysia. Tel: 06-7677798, Fax: 06-7677709. Email: [philip\\_george@imu.edu.my](mailto:philip_george@imu.edu.my)*

**Key words: Depression, knowledge, students, teachers**

**Abstract**

**Objective:** To assess the knowledge and understanding of depression as an illness amongst college students and their teachers.

**Method:** A cross sectional survey was conducted using a questionnaire with nine questions that had single best answer responses and multiple choice responses. 450 individuals of which 392 were students and 58 were teachers, from selected colleges and schools in Seremban and Kuala Lumpur were invited to participate through a process of convenience sampling.

**Results:** Eighty-nine percent of the population identified depression as a disorder that affects physical, mental and emotional aspects of a person, and 51% said that depression is more disabling than Diabetes Mellitus. Majority of participants agreed that the most important cause of depression is stressful life events. Eighty-one percent said they would seek treatment if they suffered from depression and amongst them, 45% said they would seek help from friends and family.

The majority (37% of the population) opined that yoga was the single most important aspect of treatment for depression. More teachers than students admitted that depression requires treatment, and were willing to consult someone if they suffered depression. Females were more willing to consult someone if they suffered from depression compared to males.

---

<sup>1</sup> Department of Psychiatry, International Medical University, Malaysia

<sup>2</sup> Medical Students, International Medical University, Malaysia.

**Conclusion:** Educational status does play a role in shaping beliefs about depression and its treatment. People are more comfortable consulting a friend instead of a psychiatrist if they suffered from depression. They appear to be more comfortable with non-medical means of treatment for depression. More efforts are needed to increase the understanding of depression and to reduce the stigma associated with seeing a mental health worker.

## Introduction

The World Health Organization defines Health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity".<sup>1</sup> Health literacy has been defined as the ability to gain access to understand, and use information in ways which promote and maintain good health.<sup>2</sup> Mental health literacy is defined as "knowledge and beliefs about mental disorders which aid their recognition, management or prevention".<sup>2</sup> A recent WHO survey found that depression was the fourth leading cause of disability in the world in 1990 and is estimated to be second leading cause of disability after heart disease by 2020.<sup>3</sup> WHO screened over 25 000 people in 14 countries and found depression to be the most common disorder with a prevalence of 10%.<sup>3</sup>

In Malaysia, a rural survey in 1999 reported that depressive disorders were the most common psychiatric disorders with a prevalence rate of 3.6%.<sup>3</sup> The survey discovered that people between the age group 20 to 40 have a lifetime risk of up to 20% in developing major depression.<sup>3</sup> Though the prevalence is high, doctors often fail to identify and recognise depression among their patients and often when identified, do not treat them appropriately. If left undiagnosed and untreated, depression can lead to serious complications. About 20% will develop chronic depression and 7%-10% may even commit suicide.<sup>3</sup> Early diagnosis and prompt treatment can save a patient's life. Factors that prevent early treatment include poor mental health literacy.

Depressive disorders include Major Depression, Dysthymia and Adjustment Disorder with Depressed Mood as among the most common states. Though depression is very disabling and devastating to both the patient and family, it is responsive to treatment and about 80% of patients recover with the use of appropriate medication and psychosocial interventions.<sup>6</sup>

Public awareness and understanding of depression as an illness and the available appropriate treatments are essential to ensure that the illness does not go unrecognised and untreated. Many other primary care disorders such as Diabetes Mellitus and Hypertension enjoy good knowledge and understanding among the general public who voluntarily go for screening and assessment. If a disabling illness like depression can have the same impact, more people can escape the throes of suffering and despair.

Jorm et al. (1995) assessed the Australian public's recognition of mental disorders and their beliefs about the effectiveness of various treatments (mental health literacy) through a cross-sectional survey. They used structured interviews and vignettes of a person with either depression or schizophrenia<sup>2</sup> and obtained a sample size of 2031 individuals aged 18

-74 years. One thousand-ten participants were questioned about the depression vignette and 1021 about the schizophrenia vignette. The results of the research showed that most of the participants recognised the presence of some sort of mental disorder: 72% for the depression vignette (correctly labelled as depression by 39%) and 84% for the schizophrenia vignette (correctly labelled by 27%). General practitioners (83%) and counselors (74%) received high ratings in terms of being helpful while psychiatrists (51%) and psychologists (49%) less so. Many standard psychiatric treatments such as antidepressants, antipsychotics, electroconvulsive therapy, admission to a psychiatric ward were rated as more harmful than helpful, and some non-standard treatments were rated acceptable (such as increased physical or social activity, relaxation and stress management, and reading about people with similar problems). Vitamins and special diets were rated as more helpful than antidepressants and antipsychotics. In conclusion, mental health literacy had to be improved and public understanding of psychiatric treatments needed to be raised.<sup>2</sup>

The same authors conducted a follow-up study in 2001, the outcome of which showed better understanding of depression and schizophrenia while giving more positive ratings to a range of interventions, including help from mental health professionals, medications, psychotherapy and psychiatric ward admission.<sup>7</sup> The study was conducted after a period of intervention to improve the knowledge and understanding of these two disorders. This change will surely have positive implications for help-seeking and treatment practices.

Our study was conducted among students and teachers at selected tertiary educational facilities in Seremban and Kuala Lumpur and was aimed at assessing their understanding and knowledge of depression. It was also used to assess differences between the two populations surveyed.

## **Methodology**

This is a cross sectional study conducted from August to December 2006. Participants were required to provide a brief demographic profile. There was no collection of personal data that could be used to identify participants and strict confidentiality was maintained throughout the study. A questionnaire consisting of 9 questions was developed (Appendix 1) for the purpose of the study. The questions target different areas of knowledge and understanding with regards to Depression. Question 1 attempts to discover how many participants have relatives suffering from depression. Questions 2, 3, 4 and 5 assess the understanding and knowledge of depression while Questions 6, 7, 8 and 9 assess help-seeking behaviours as well as popular modes of treatment.

The colleges and universities where the questionnaires were distributed were selected randomly and a convenience sample of the participants chosen. A total of 450 copies of the questionnaire were distributed and the responses analysed using the Chi-square method. Confidentiality was maintained and sealed collection boxes were provided for participants



to drop in the forms after completing them. Names of the institutions were also not disclosed.

## Results

A total of 450 completed questionnaires were analysed. Eighty-three percent of the sample population indicated they do not have relatives suffering from any mental illnesses. Eighty-nine percent of the sample population defined depression as “a type of disorder that affects the physical, mental and emotions of the patient”, while the rest did not have proper or accurate knowledge on depression.

For the question regarding the lifetime prevalence of depression, 42% correctly chose a prevalence of “10%” while 28% chose “three percent” and 19% chose “20%”. 51% of the sample population felt that depression was more disabling than Diabetes Mellitus. Seventy-one percent of the sample population felt that the most important cause of depression was “stressful life events”, followed by factors such as “genetic inheritance”, and finally “weak personality”.

Seventy-four percent believed that depression requires some sort of treatment while 81% would have sought treatment if they were suffering from depression. Of the total population that had chosen to seek treatment, 46% would have sought help from friends and family, whilst 20% from a psychiatrist and 17% from a psychologist. Thirty-seven percent of the sample population believed that yoga was the single most important aspect of treatment for depression, 29% chose exercise and only 18% considered antidepressant medication.

The following section compares answers provided by the students and their teachers/lecturers, as well as the differences in mental health literacy and opinions between male and female participants. Chi-square analyses ascertained if the differences between the responses between the two groups were significant, using a value of  $p < 0.05$ .

### ***Comparison between students and teachers/lecturers***

16.8 percent of students and 15.5 % of lecturers had relatives who were suffering from some form of mental diseases. 91.4 percent of lecturers had defined depression correctly compared to students (88.5%). Analysis score was  $p = 0.808$  ( $> 0.05$ ), showing no significant difference between the two groups. Lecturers significantly underestimated the prevalence of depression with 19% identifying that it affected roughly 10% of the population compared to 44% of students ( $p < 0.005$ ). (Figure 1)

Both students and teachers identified that depression was more disabling than Diabetes Mellitus. They also believed that stressful life events were the single most important cause of depression. Figure 2 shows their responses to medical treatment for depression. More teachers (89.7%) than students (71.6%) responded saying that depression required medical treatment and this was found to be statistically significant ( $p < 0.05$ ).

91.4 percent of lecturers would have consulted someone if they suffered from depression while 75.9% of students would have sought treatment if they suffered from depression. Statistical analysis obtained a significant score of  $p=0.032$ .

Figure 3 indicates that 49.1% of teachers as compared to 15% of students would have most likely a consulted a psychiatrist if they suffered from depression and. Students preferred to seek help from friends and family. This calculation also proved statistically significant ( $p<0.005$ ).

Figure 4 highlights responses in relation to the best perceived treatment for depression. Among the teachers, the first choice of treatment for depression was antidepressant medication (47.4%) with yoga as second choice (33.3%) as compared to first choice of yoga among students (37.5%) followed by exercise (31.1%). The differences between the two groups was again significant with a score of  $p<0.05$ .

### ***Comparison between genders***

It was observed that 87.1% of females would have consulted and sought treatment if they suffered from depression compared to 74.2% of males. This result was statistically significant ( $p < 0.05$ ) (Figure 5).

### **Discussion**

Whilst it is important to be equipped with knowledge on physical diseases, knowledge on mental disorders or mental health literacy in comparison has been neglected. People with mental illnesses often in Malaysia are often scorned upon and marginalised. This increases their suffering and reduces accessibility to effective treatments. Many people in Malaysia suffering from depression present very late into their illness to the mental health worker. This reduces their chances of recovery and increases the burden on themselves, their family and the community at large.

Generally the public cannot recognise specific disorders or different types of psychological distress. They often differ from mental health experts in their beliefs about the causes of mental disorders and the most effective treatments.<sup>10</sup> Attitudes which hinder recognition and appropriate help-seeking are common. Much of the mental health information most readily available to the public is misleading. However, there is evidence that mental health literacy can be improved.

This survey conducted among teachers and students at different colleges and universities around Seremban and Kuala Lumpur aimed at assessing how depression is understood by teachers and students and then to compare the two samples. Almost 90% of the population sample in this study were able to identify appropriate definitions for depression as an illness. Its prevalence was better identified by students compared to teachers suggesting that mental health issues may be more relevant and acceptable among the younger generation. Only half of the population surveyed felt that depression was more

disabling than Diabetes Mellitus, suggesting a lack of knowledge of the effects of mental illness. Patients or families of patients who believe that their illness is not disabling may present for help at much later stages of their illness. This may hinder recovery and increase complications from depression such as suicide and chronic depression.

A higher percentage of teachers were willing to consult someone if they suffered from depression. They admitted the need for treatment which indicated that this segment of the population had a better understanding of the seriousness of depression. Educational status may play a role in the understanding of depression as a whole, and the need for its treatment.

Students preferred yoga as a method of treatment while teachers preferred antidepressant medications. Again, the choice may differ among the age groups or those with different educational status. This result may suggest difficulties that young adults may face in accepting medical treatments for their depression. It further suggests supervision of treatment regimens is essential during adolescence and early adulthood. Teachers chose to seek help from psychiatrists compared with students. Students reported feeling more comfortable seeking help from friends or family. This emphasises the importance of treatment for common mental conditions which should be made available in primary care and general practice, and families empowered to recognise and understand depression as an illness.

This survey found that more females would consult someone if they had depression compared with males. This may explain the 2:1 ratio difference among female and male prevalence of depression. It also suggests that females may be more willing to discuss their feelings and emotions with others compared to males.

### **Limitations**

As this study was conducted over 9 years ago, changes in mental health literacy among Malaysian students and teachers might have improved over time with government and media efforts, hence it may be worthwhile to replicating the survey and compare those changes reflected over a 10-year period. Secondly, our sample population was from tertiary education facilities and may not reflect the mental health literacy in a lower educational cohort.

### **Conclusion**

Mental health literacy differed between teachers and students, as well as between genders. Overall, knowledge and understanding of depression was better than expected but the acceptance of appropriate treatment for depression seemed to be lacking. Improving the public's literacy on depression could augur well with better acceptance of evidence-based mental health care.

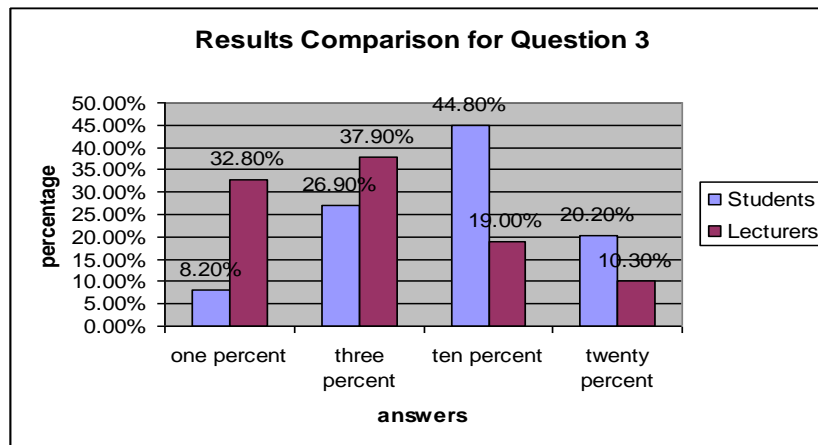
Poor mental health literacy can also affect people with common mental disorders who may be denied effective self-help, in addition to them not receiving the appropriate support

measures from the community. There is thus a need to build on research in this area and to introduce the concept of mental health literacy to the public and highlight interventions to improve acceptability and appropriate health-seeking behaviour for those with mental illnesses in Malaysia.

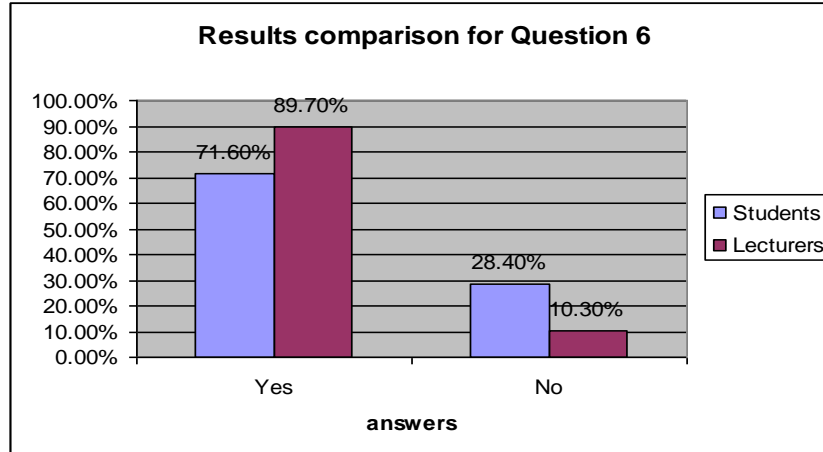
## References

1. Aboud FE. Health psychology in a global perspective, Sage Publications. California, 1998; 244.
2. Jorm AF, Korten AE, Jacomb PA, et al. Mental health literacy: a survey of the public's ability to recognize mental disorders and their beliefs about the effectiveness of treatment. Medical Journal of Australia 1997; 166: 182-6.
3. Suzanna JAA, Norlaili MT, Sherina MS. The prevalence of depressive disorders among adult patients attending primary care clinics. Malaysian Journal of Psychiatry. September 2005; 13(2):.....
4. The Star Online, March 31 2006. Students launch anti-suicide drive. Available from: <http://thestar.com.my/services/printerfriendly.asp?file=/2006/3/31/central/13783930.asp&sec=central>
5. Psychology information online, Depression – information and treatment (document on the internet) New Jersey (cited 12<sup>th</sup> July 2006), available from: <http://www.psychologyinfo.com/depression>
6. Kiloh LG, Andrews G, Neilson M. The long-term outcome of depressive illness. British Journal of Psychiatry 1988; 153: 752-7.
7. Anthony F J, Christensen H, Griffiths KM. The public's ability to recognise mental disorders and their beliefs about treatment: changes in Australia over 8 years. Australian and New Zealand Journal of Psychiatry 2006; 40: 36-41.
8. The Star Online, 11<sup>th</sup> August 2006. Stigma attached to mental illness an obstacle. Available from: <http://thestar.com.my/services/printerfriendly.asp?file=/2006/8/11/nation/15109344.asp&sec=nation>
9. The Star Online, 22<sup>nd</sup> May 2006. Mental disorders afflict 21% of Malaysians. Available from: <http://thestar.com.my/services/printerfriendly.asp?file=/2006/5/22/nation/14312648.asp&sec=nation>
10. Jorm AF. Mental health literacy: public knowledge and beliefs about mental disorders. The British Journal of Psychiatry 2000; 177: 396-401.

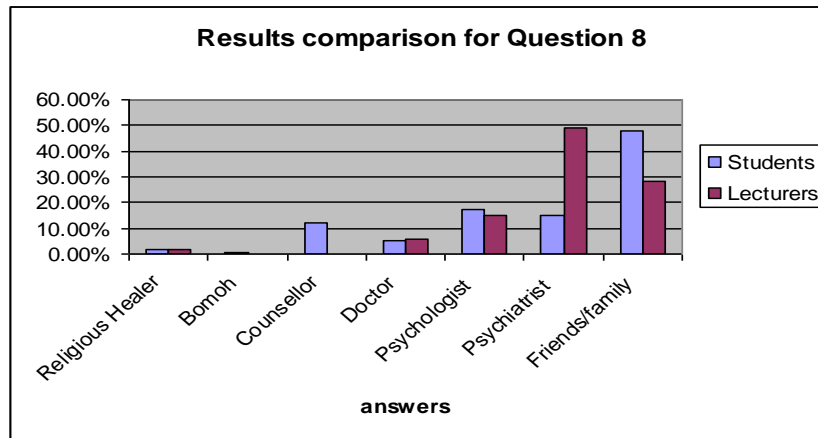
**Figure 1 “How common is depression in the population?”**



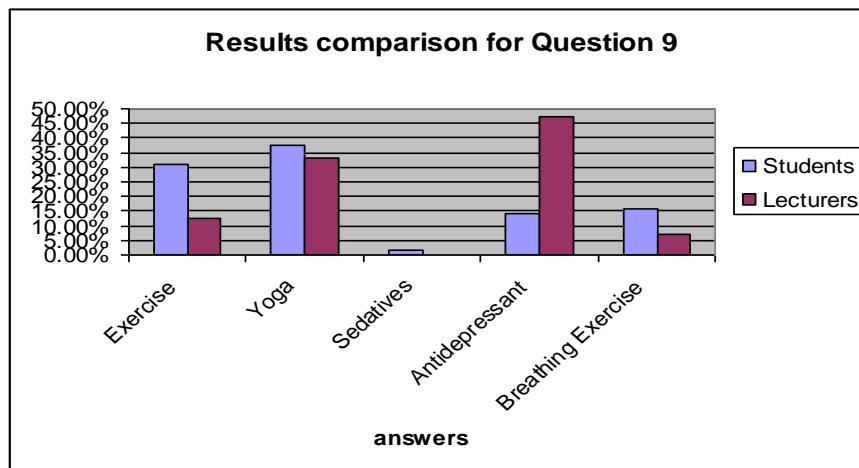
**Figure 2 “Do you think depression requires medical treatment?”**

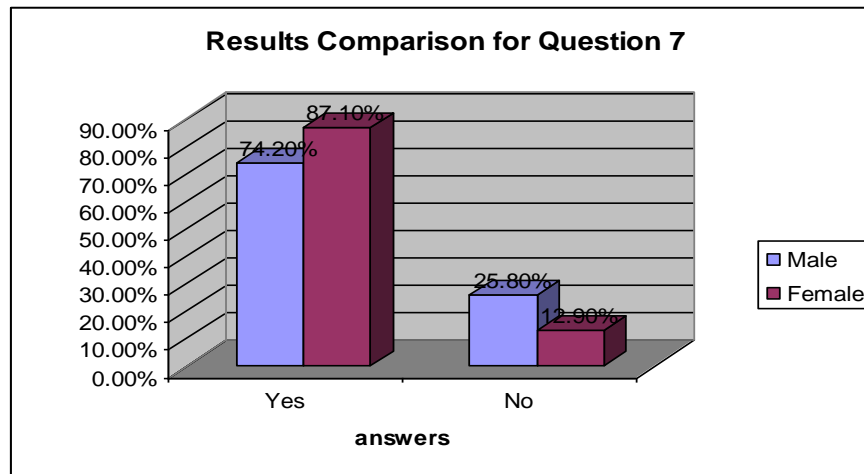


**Figure 3 If yes to seeing someone if you had depression in question 7, “Who would you see?”**



**Figure 4 “Most important aspect of treatment for depression”**



**Figure 5 “Would you consult anyone if you had depression?”**

### Appendix 1 – Questionnaire

Please state whether you are: ( ) Student or ( ) Lecturer / Teacher

Age: \_\_\_\_\_ Gender: ( ) Male ( ) Female

**Please do not give any personal identification details in this questionnaire.**

*Please choose a single best answer for each question, and tick the appropriate box.*

1. Have you any relatives suffering from a mental disorder?

( ) Yes ( ) No

2. What is Depression?

- ( ) A type of disorder where a person finds some difficulty in differentiating between what is real and what is not.
- ( ) A type of disorder that affects physical, mental and emotional aspects of someone. It affects the person's appetite, sleep, self-perspective and mindset.
- ( ) Weakness in an individual due to low self-esteem and lack of discipline.



3. How common is depression in the population?

- ☐ Lifetime prevalence of 1%
- ☐ Lifetime prevalence of 3%
- ☐ Lifetime prevalence of 10%
- ☐ Lifetime prevalence of 20%

4. Is Depression more disabling compared to other disorders such as Diabetes Mellitus?

- ☐ Yes      ☐ No

5. What is the single most important cause that you feel contributes to Depression disorder?

- ☐ Genetics; more likely if the family member has it.
- ☐ Medication.
- ☐ Stressful life events.
- ☐ Having committed a bad deed / sin.
- ☐ Having a weak personality.

6. Do you think depression requires medical treatment?

- ☐ Yes      ☐ No

7. Would you consult anyone if you had depression?

- ☐ Yes      ☐ No

8. If yes to above Q7, who would you see?

- ☐ Religious healer      ☐ Doctor      ☐ Friends / family
- ☐ Bomoh      ☐ Psychologist
- ☐ Counselor      ☐ Psychiatrist

9. Of the following, mark the most important aspect of treatment for depression

- ☐ Exercise      ☐ Anti depressant medication
- ☐ Yoga      ☐ Deep breathing exercise
- ☐ Sedatives

---

*End of questionnaire*

**CASE REPORT**

# Cerebral Venous Sinus Thrombosis Secondary to Nephrotic Syndrome in an Adult: a Case Report

SML Tai<sup>1</sup>, ELT Choon<sup>2</sup>

---

*Corresponding author: Dr. Mei-Ling Sharon Tai, Division of Neurology, Department of Medicine, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia. Email: [sharont1990@gmail.com](mailto:sharont1990@gmail.com)*

**Key words:** Cerebral venous sinus thrombosis, Nephrotic syndrome, stroke

**Abstract**

**Introduction:** Cerebral venous sinus thrombosis (CVST) is uncommon and presents a diagnostic challenge due to its variable presentation pattern.

**Case report:** A 55 year old male presented with acute onset of headache and dizziness. MRI of brain showed venous infarcts at the right posterior temporal and left medial temporal lobes secondary to CVST. Magnetic Resonance Venography (MRV) showed thrombosis at the anterior two-thirds of superior sagittal sinus, right transverse, sigmoid sinus and right internal jugular vein. The 24-hour urine protein was found to be raised. Early recognition aided the diagnosis of CVST and treatment started within a week. He thereafter improved rapidly after anticoagulation treatment.

**Conclusion:** This report highlights the importance of prompt diagnosis of CVST via neuroimaging and the benefit of immediate anticoagulation therapy in its management.

**Introduction**

Cerebral venous sinus thrombosis (CVST) is an uncommon medical condition. It occurs in 3-4 per million people annually. Any age group may be affected, although it is said to be more common in the third decade of life.<sup>1,2</sup> CVST can cause a diagnostic challenge for clinicians and its clinical presentation is varied, comprising of headache, vomiting and

---

<sup>1</sup> Department of Medicine, University of Malaya, Kuala Lumpur

<sup>2</sup> Hospital Angkatan Tentera Tuanku Mizan, Kuala Lumpur.

seizures. We present a rare case of a middle-aged man with CVST secondary to Nephrotic syndrome.

### Case Report

A 55 years old male with a background history of Type II diabetes mellitus and hypertension for 17 years on follow-up with general practitioner was referred from a private hospital with complaints of persistent acute onset headache and dizziness for a two-day duration. According to family members, the he became easily forgetful and occasionally confused. There was no fever, blurring of vision or neck pain. Nor was there any fainting episodes, speech impairment or limb weakness. His medications were T. Metformin 500mg BD, T. Glibenclamide 5mg BD and T. Propranolol 40mg OD.

On examination, he was found to be alert and conscious. Glasgow coma scale (GCS) score was 15/15 and he did not display any signs suggestive of meningism. His level of hydration was adequate. Blood pressure was 202/111 mmHg and pulse rate 84 beats per minute. He was not tachypnoeic and did not have pedal edema or ascites. Fundal examination was normal. Neurological examination of cranial nerves, upper limbs and lower limbs was normal. He did not have cerebellar signs or diplopia. Cardiovascular, respiratory and abdominal examination was unremarkable. He also did not have leg swelling that pointed to deep venous thrombosis.

Computed Tomography (CT) of the brain showed hypodense lesions at the right posterior temporal lobe and the left anterior temporal lobe, duly reported as two intraparenchymal temporal lobe lesions.

Urine FEME showed proteinuria of 4+ on admission. Blood investigations revealed raised serum urea (11.2 mmol/L) and serum creatinine (226 mmol/L) levels. Serum total protein was 70 g/L and serum albumin was 31 g/L. His corrected serum calcium level was also elevated (2.71 mmol/L). Other relevant blood test results were normal. Electrocardiogram showed sinus rhythm of 85 beats per minute.

He was initially diagnosed as having a hypertensive crisis at the Emergency Department considering his blood pressure was more than 180/100mmHg with a corresponding increase in his urea and creatinine levels that suggested acute renal impairment. A differential diagnosis of stroke was also entertained. He was given T. Amlodipine 10 mg as a stat dose and was reviewed the following day by the neurology team and diagnosed as having a possible posterior circulation stroke in lieu of the acute onset of headache and dizziness. Subsequently, T. Aspirin 100mg OD and T. Simvastatin 40mg ON was started after diagnosis of a haemorrhagic stroke was ruled out. Subcutaneous Actrapid 6 units TDS and Insulatard 6 units ON were also administered.

Magnetic Resonance Imaging (MRI) of the brain reported features suggestive of encephalitis and cerebral oedema; however, the image was degraded by motion artefacts

and it was recommended that the MRI be repeated with the patient sedated. In the meanwhile, lumbar puncture was performed to rule out central nervous system infection. Cerebrospinal fluid (CSF) opening pressure was raised at 39 cm H<sub>2</sub>O and closing pressure was 21 cm H<sub>2</sub>O. IV Acyclovir was initiated to treat possible viral encephalitis. CSF biochemistry, Gram stain, bacterial culture & sensitivity, viral serology, acid fast bacilli (AFB) direct smear and AFB culture & sensitivity were reported to be normal. A Repeat MRI of brain was performed with sedation and found an acute infarct (venous) at the right posterior temporal and left medial temporal lobes secondary to CVST (Figures 1a and 1b). This raised the clinical suspicion of CVST and considering he showed poor clinical response to initial treatment administered, Magnetic Resonance Venography (MRV) was carried out and revealed thrombosis at the anterior two-thirds of superior sagittal sinus, right transverse, sigmoid sinus and right internal jugular vein (Figures 2a and 2b). Magnetic Resonance Angiography (MRA) done for completion's sake was found to be normal. Anticoagulation with IV Heparin, overlapping with oral Warfarin was commenced. T. Perindopril was added to his treatment regime as his blood pressure was still considerably high (180/104 mmHg) and the latter was subsequently well-controlled with a dose of 2 mg OD.

A diagnosis of Nephrotic syndrome was made based on a significantly raised 24-hour urine protein (5.93g/24 hours) on day 4 of hospitalization. He also had hypercholesterolaemia with fasting lipid profile (FLP) results being total cholesterol 9.7 mmol/L, LDL 7.27 mmol/L, HDL 1.29 mmol/L and triglycerides 2.5mmol/L. On day 7 of hospitalization, serum total protein had reduced to 65 g/L and serum albumin 26 g/L. Serum urea at the time was 7 mmol/L and creatinine level was 201 mmol/L.

Ultrasonography of the kidneys revealed normal kidney size bilaterally with normal echogenicity. Ultrasound Doppler of the same showed no thrombosis of the renal blood vessels. Other investigations like CT of the thorax, abdomen and pelvis to rule out other causes of CVST such as malignancy proved negative. Thrombophilia screen that consisted of anti-thrombin III, protein C, protein S and anti-cardiolipin antibody was normal.

Following the diagnosis of Nephrotic syndrome, he was referred to the nephrology team. A renal biopsy suggested to investigate the aetiology was cancelled due to concerns pertaining to the risk of renal hemorrhage given the concurrent anticoagulation therapy. Nevertheless, the success of the anticoagulation therapy rendered led to an improvement in his condition. The intensity of his headaches reduced markedly and he was discharged 20 days after hospitalization with no new complaints. As his INR was 1.9 whilst on oral Warfarin 7 mg OD, IV Heparin was hence stopped.

On follow-up six months later, he complained of occasional dizziness but no worsening of headache intensity. Neurological examination was normal. Repeat MRI of brain seven months later showed improvement of cerebral venous thrombosis with no new infarcts. Repeat MRV at the time still showed residual thrombosis at the right transverse sinus and

anterior two-thirds of superior sagittal sinus. Both neuroimaging investigations were again repeated a month later and showed no further changes.

He was then reviewed in the INR clinic to monitor his compliance to warfarin and the INR level was found to be within therapeutic range. He was given the needful advice with regards to its interaction with certain foods and other medications, as well as caution to seek treatment if he developed bleeding of any form. Oral Warfarin therapy was continued for eight months at the same dose. He continued to have nephrotic syndrome with persisting proteinuria despite the fasting lipid level normalizing; the latest serum albumin was 46 g/L (normal). He did not develop a recurrence of his initial symptoms of headache, dizziness, forgetfulness and confusion and did not have renal biopsy, nor given steroids.

## Discussion

The interesting phenomenon extensive CVST has been reported in medical literature. However, the age group (55 years), together with gender of our patient (male), was unusual and made the diagnosis more challenging. CVST is usually found amongst young adults and is three times more common among women aged between 20 and 35.<sup>1,2</sup> The use of the oral contraceptive pills (OCP), pregnancy and post-partum complications makes them more susceptible.<sup>1</sup> At least one risk factor can usually be found in 85% of patients with CVST.<sup>2</sup> Other than pregnancy and OCP use, more common causes for CVST are thrombophilia and infections such those of the central nervous system and mastoiditis.<sup>2</sup> Other risk factors for its development include vasculitis, malignancy, inflammatory bowel disease and haematological disorders such as polycythaemia rubra vera and paroxysmal nocturnal hemoglobinuria.<sup>2</sup>

The most common clinical features of CVST (Table 3) are headache, seizures, hemiparesis and loss of consciousness.<sup>3</sup> Our patient did have headache, no seizures or limb weakness and the short duration of occasional confusion was not typical of CVST. Thrombophilia is present in 34% of CVST patients<sup>4</sup> and of these, inherited thrombophilia is observed in 22%.<sup>3</sup> Inherited thrombophilias include deficiencies of antithrombin III, protein C, protein S, factor V Leiden mutation and prothrombin gene mutation 20210.<sup>4</sup> The acquired thrombophilias are associated with antiphospholipid antibodies and hyperhomocysteinemia.<sup>4</sup>

The pathogenesis of CVST can be due to two major mechanisms. Firstly, it can result in raised venular and capillary pressure, leading to decreased cerebral perfusion pressure, cerebral oedema and breakdown of the blood-brain barrier. In addition, venous and capillary rupture can result in intra-parenchymal bleed. The other pathophysiological mechanism is obstruction of cerebral venous sinuses, resulting in less CSF absorption and an increase of intracranial pressure.<sup>2</sup>

CVST in adult patients with Nephrotic syndrome is very uncommon with approximately only 35 cases reported in the literature thus far.<sup>3</sup> The other reported patients with

nephrotic syndrome and CVST had blood urea/creatinine ratios (BUN/Cr ratio) of 42.9 to 44,<sup>5</sup> whereas ours had a higher BUN/Cr ratio of 49.6. Although CVST is commoner in children with nephrotic syndrome,<sup>6</sup> the diagnosis nevertheless requires a high index of suspicion due to its non-specific clinical features.<sup>3</sup> As this disease can cause serious neurological complications which may lead to significant morbidity and mortality, early diagnosis remains crucial.<sup>3</sup>

The formation of CVST in nephrotic syndrome is due to a relative hypercoagulable state.<sup>3</sup> The most important contributory factors of hypercoagulability are protein S, protein C and antithrombin III deficiency.<sup>7</sup> Next important contributory factors are raised levels of Factor III, Factor V alpha-2, antiplasmin,  $\gamma$ -fibrinogen and fibrinopeptides. When the levels of these factors are increased, this results in hypercoagulability and subsequently, CVST.<sup>7</sup> Fibrinopeptide A encourages the formation of protofibril to produce fibrillar pattern in the developing thrombus and  $\gamma$ -fibrinogen has an antithrombotic role by way of thrombin sequestration.<sup>8</sup> Other less common causes of CVST are immune complexes formation, volume depletion, dehydration and hypoalbuminaemia.<sup>7</sup> The treatment of CVST such as corticosteroids and diuretics can also increase the risk of its development in patients with Nephrotic syndrome.<sup>7</sup>

The treatment of patients with CVST with low molecular weight heparin or intravenous heparin should commence within the first two weeks of the onset of disease.<sup>3</sup> Oral anticoagulation with oral Warfarin may be given for three months if CVST is secondary to a transient risk factor, and for six to 12 months in patients with idiopathic CVST.<sup>3</sup> In our patient, Warfarin was preferred to Heparin as outpatient treatment because of its once daily dosing and ease of administration by way of a tablet instead of a subcutaneous injection. In contrast, low-molecular weight heparin requires twice daily subcutaneous administration – however, it has less side effects and does not require INR monitoring.

The prognosis of CVST varies from complete recovery to death.<sup>9</sup> The reported mortality rate ranges from 6 – 15%.<sup>10</sup> In one case series of 11 patients with CVST in Nephrotic syndrome, two patients died, seven recovered completely and one patient had residual neurological deficits.<sup>3</sup> This emphasises our concern for early detection and thence, appropriate anticoagulation therapy.

## Conclusion

A diagnosis of CVST needs to be considered in patients with Nephrotic syndrome who develop neurological signs or deficits. A high index of suspicion, early diagnosis of CVST with MRV and rapid commencement of anticoagulation often results in excellent outcomes whilst avoiding fatal consequences.

## References

1. Stam J. Thrombosis of the cerebral veins and sinuses. *N Engl J Med* 2005; 352:1791–8.
2. Piazza G. Cerebral venous thrombosis. *Circulation*. 2012 Apr 3; 125(13):1704-9.
3. Xu H, Chen K, Lin D, Dai L, Chen H, Xu Z. Cerebral venous sinus thrombosis in adult nephrotic syndrome. *Clin Nephrol* 2010 Aug; 74(2):144-9.
4. Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke* 2004; 35:664–70.
5. Gera DN, Yadav DK, Kute VB, Patil SB, Trivedi HL. Cerebral venous sinus thrombosis in children with nephrotic syndrome. *Indian J Nephrol* 2012 Nov; 22(6):455-8.
6. Suri D, Ahluwalia J, Saxena AK, Sodhi KS, Singh P, Mittal BR, Das R, Rawat A, Singh S. Thromboembolic complications in childhood nephrotic syndrome: a clinical profile. *Clin Exp Nephrol* 2014 Oct; 18(5):803-13.
7. Harris RC, Ismail N. Extrarenal complications of the nephritic syndrome. *Am J Kidney Dis* 1994; 23:477-97.
8. [John C. Chapin](#), [Katherine A. Hajjar](#). Fibrinolysis and the control of blood coagulation. *Blood Rev* 2015 Jan; 29(1): 17–24.
9. Ferro JM, Canhao P, Stam J et al. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke* 2004; 35:664-70.
10. Hameed B, Syed NA. Prognostic indicators in cerebral venous sinus thrombosis. *J Pak Med Assoc* 2006; 56: 551-4.



**Figure 1a** MRI T2W showing hyperintense lesions at left medial temporal area and right posterior temporal area

**Figure 1b** MRI Diffusion weighted image (DWI) showing restricted diffusion at left medial temporal area and right posterior temporal area

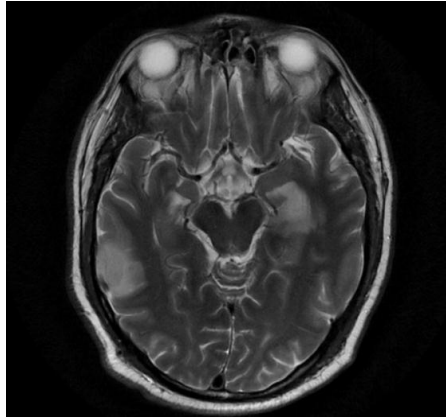


Figure 1a

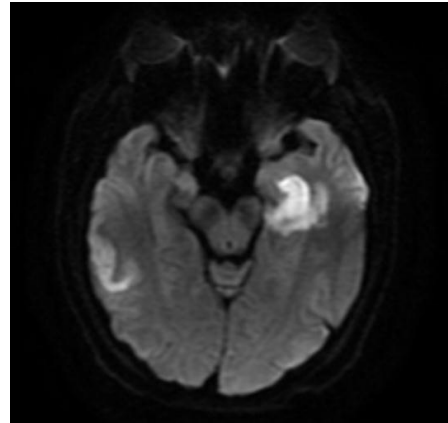


Figure 1b

**Figures 2a and 2b** MRV showing thrombosis at the anterior two third of superior sagittal sinus, right transverse, sigmoid sinus and right internal jugular vein

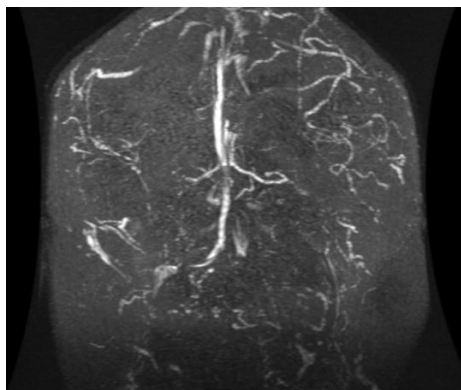


Figure 2a

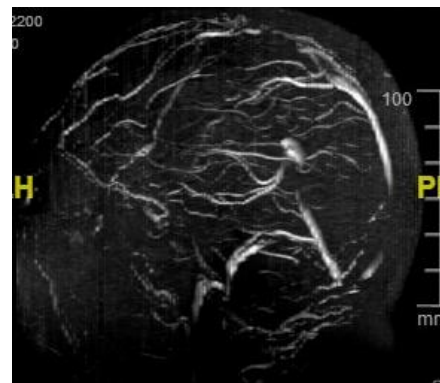
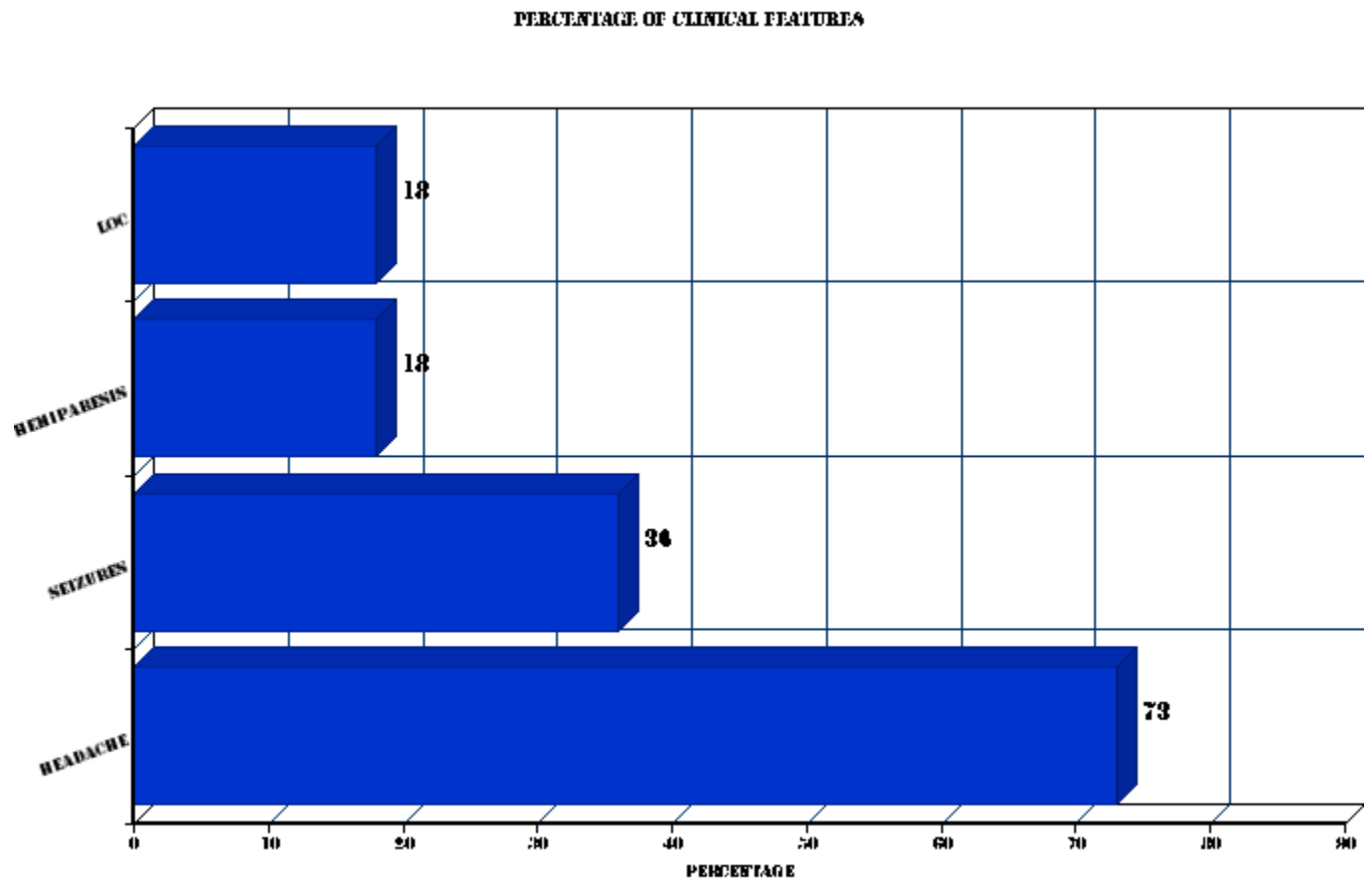


Figure 2b

**Table 1 Clinical features of CVST**

# Submission of Articles

---

The articles for publication in the journal may be kindly sent to The Editor <masheditor@gmail.com>. The article should be prepared as per the **Manuscript Submission** guidelines given below:

- (i) The article should be in internationally accepted English
- (ii) Title Page: Title of manuscript , Name(s) and affiliation of author(s), institution(s) and city(ies) and address of corresponding author (Tel., Fax & E-mail)
- (iii) Abstract should highlight objectives, methods, results, conclusion (except Review Articles and Case Reports, where it could be content-specific)
- (iv) Article (double-spaced in Word format) should be headed by introduction, material & methods, results and, discussion.
- (v) References (maximum number of references for update article – twenty (20), original article – ten (10) and case reports – six (6) preferably). This would be in accordance with the Vancouver system.
- (vi) Table/graphs: Each on separate file (maximum number of tables/graphs – four (4) in original articles).
- (vii) Photographs: Each also in separate file (maximum number of photograph files - three (3) for original article and one to two (1-2) for case report.

## Advertising in the MASH Journal

---

The journal site will offer a wide range of advertising opportunities to pharmaceutical firms, equipment/instrument manufacturers at reasonable rates (provided there is no breach of ethics as in accordance with advertising laws):

Front Cover (Inside)	RM 3,000/-
Back Cover (Outside)	RM 2,000/-
Back Cover (Inside)	RM 1,500/-
Full Page	RM 4,000/-
Half Page	RM 2,500/-
Website advertisement (6-monthly)	RM 1,000/-

Contact: <masheditor@gmail.com>