

Illness Representations, Psychological Distress, Posttraumatic Stress Symptoms on the Physical Recovery From Stroke : A Study Protocol

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ABSTRACT

There has been extensive research to look at the pharmacological effects on immediate recovery after stroke. However, there is lack of research to investigate the contributions of other effects that influence recovery after stroke. The study aims is to determine the extent of psychological factors such as illness representations, perceived control, psychological distress and posttraumatic stress symptoms in predicting recovery from disability following stroke. A cross sectional and longitudinal study with two times lines (six weeks and six months post-stroke) will be conducted in this study. It will consists of 180 patients from UKM Medical Centre. The idea of enhancing recovery from disability through the usage of psychological variables is important to assist recovery despite depending on a fully medical approach. Hence, it will provide information to the healthcare services and the government to improve the services and treatment intervention of the stroke sufferers.

INTRODUCTION

Strokes are the third leading cause of mortality worldwide (WHO, 2001) and have been projected to be the third leading cause of mortality in 2030 after cancer and ischemic heart attack (WHO, 2007). Strokes are also known to be the primary cause of physical disability (WHO, 2001). The number of people living with strokes will rise in the future since the population is aging and stroke survivors are living longer (Bonita, Solomon, & Broad, 1997). These situations may lead to a growing incidence of strokes with an increase in the numbers of people with residual disability. With these consequences, strokes could cause extreme pressure on the health and social services (Wade & Langton Hewer, 1987).

In Malaysia, there is limited information on the rate of mortality and morbidity of stroke. However the Malaysian Ministry of Health 2008, reported that stroke was on the fifth list causing death in the Ministry of Health Hospitals with mortality rate of 8.65 per 100,000 population, after heart diseases & diseases of pulmonary circulation, septicaemia, malignant neoplasms, pneumonia (MOH, 2008). This shows that the mortality of stroke is somewhat controllable; however there is no information on the morbidity of stroke being reported. These situations may lead to growing numbers of people with residual disability. A review by Aziz & Raymond (2008) stated that a new avenue and intervention involving care and evidence based medicine of managing further rehabilitation should be studied in stroke patients which can fit into our social and cultural way of life. With regards to this, the researcher will emphasize on the avenue which consists of psychological variable which might predict in maintaining or decreasing disability.

Despite that, Caro, Huybrechs, and Dunclease (2000), reported lifetime cost per patients are estimated between US\$59, 800 to US\$230,000 and now the cost of treatment nearly double of the expenditure. Even by the year 2020, according to WHO (2000) stroke and coronary artery disease together are expected to be the leading causes of lost healthy life years. Due to this, it is important for a study to be conducted in this area to assists the government to reduce the burden. Although there is no specific figure of expenditure of stroke have been highlighted in Malaysia, great attention should be given to the above figure. Prevention movement and medical treatment are areas that certainly be focused by the government however, contribution to take care of stroke survivors from relapse are also important. In other words, by exploring research in the area of health psychology to manage stroke patients with disability will benefit the government in terms of reducing the economical burden and increase social functioning among stroke sufferers.

In this study, the research will be based on the model by Johnston et al (1999, 2007) on the recovery from disability following strokes as well as collaboration with few other studies. In this study, we explore one new variable that can predict recovery due to stroke known as posttraumatic stress symptoms (PTSS). Until now less than five researches have been done to look at the function of PTSS among stroke patients (Ezzat, et. al, 2011). Most of the studies only screen PTSS and diagnosed Posttraumatic Stress Disorder without any investigation on its contribution through recovery. However this study will examine the influence of all these variables in predicting disability.

A few previous studies have addressed the role of psychological variables such as social-cognitive variables in predicting recovery from disability and predictive validity has been demonstrated in prospective studies for a range of variables including recovery locus control (Johnston, Pollard, Morrison & MacWalter, 1999), illness representations (Hagger & Orbell, 2000) and social support (Wilcox, Kasl, & Berkman, 1994). Despite that, psychological approaches to disability have placed considerable importance on the role of emotional distress in influencing level of disability. Fisher and Johnston (1999) have demonstrated that experimentally manipulating emotion state can alter short term disability in a predictable manner. Patients whose anxiety levels were increased using a mood induction procedure became more disabled, while those whose anxiety was reduced became less disabled.

Following to that, psychological variables are considered to be important factors in reducing disability. Therefore, Aziz and Raymond (2008) suggested new researcher to investigate the psychological factors in predicting recovery through rehabilitation. Therefore, it is important to study the contribution and influence of these variables in Malaysian context so that we can formulate the intervention strategies to assist stroke survivors with disability to enhance recovery.

In addition, the interest that evokes research in this area is due to the increasing numbers of survivors of the life-threatening illness. The vast majority of individuals treated will be living for some extended period of time with the disease. This may lead to a wide range of investigation to know what factors contribute to longevity of age among survivors. Despite that, psychological distress among survivors has been highly reported. However, stressor that enhances the development of the psychological distress varies. This is explained by the Common Sense Self-Regulation Model and Health Belief Model in Health Psychology. As an example, studies on breast cancer survivors noted that the threat associated with cancer is primarily the information that one has about the disease. In this sense, the diagnosis of cancer is similar to learning that one has been exposed to radioactive or toxic chemical contamination (Green, et al., 1998). The stressor in this case is the information that one has been exposed or has cancer or heart damage, which is learned after the fact. These differences in the nature and source of the threat have important diagnostic implications. Specifically, the intrusive images and thoughts about the threat may not be actual recollections of the events, such as precise moment of receiving news that one has cancer, but more future-oriented rumination about possible recurrence, that manifest the physical problems, or death.

The impact of PTSS on physical health is not widely investigated but has become an interesting area to explore (Buckley, Green & Schnurr, 2004). Indeed, when examining how stress related to trauma, PTSS and life-threatening illness, it rises a number of interesting questions such as : Does the experience of psychological trauma have an adverse effect on physical health? Or can receiving a terminal medical diagnosis serve as a life-threatening experience which gave the same impact such as experiencing external trauma like rape and combat. With these interesting questions, it motivates the development of potential research in this area. In addition, with the sophisticated medical treatment today lead to the recovery and decrease the mortality rate may develop a psychological effect to the survivors such as depression, lack of social support or even mood problems. Tremendous effect can occur if the life-threatening illnesses lead to disability

Posttraumatic stress symptoms are the new emotional predictors that will be introduced in this study. Posttraumatic stress symptoms (PTSS) are symptoms related to Post-traumatic stress disorder (PTSD). They consist of intrusion (e.g. recurrent re-experiencing of the events); avoidance (e.g. actively denying or not thinking about the stroke); and hyperarousal (e.g. become highly anxious). Three studies reported that stroke patients suffer from PTSS. Sembi, et al. (1999), found 21%, Bruggimann et al. (2006) found 31% and Merrimann, Norman, and Barton, (2007); found 30.7%., of PTSS in stroke patients. Such high figures indicate the importance of examining the effects of PTSS in predicting recovery from disability.

To recapitulate, we believe that the illness representations, perceived control, psychological distress along with posttraumatic stress symptoms have their own roles to predict physical recovery among stroke patients. This research is important to assist the pharmacology evidence in helping the stroke patients with physical disability become functional in their daily activity and can reduce the burden of the family, social and the government. Evidence shows that early medical treatment is important to reduce disabilities however other factors such as family, social and also psychological cannot be ignored. Even, the ICF formulation clearly recognizes the potential role of psychological, behavioral, social and contextual factor and indicates their relevance to disabling conditions. The researcher also will synchronize the result from this study to develop an appropriate intervention in the future so that it can be used to assist stroke survival to reduce their disability.

Therefore, the aim of this study is to investigate the extent of psychological factors namely illness representations, perceived control, psychological distress and posttraumatic stress symptoms in predicting physical recovery following stroke.

METHOD

Design

It is a combination between cross sectional and longitudinal study with two times lines (six weeks and six months post-stroke).

Sample Size

We will recruit one hundred and thirty (130) patients with a confirmed diagnosis of stroke at UKM Medical Centre at six weeks post stroke. Total patients being recruited will amount to 130. For this study, there are ten (10) psychological variables (timeline acute; timeline chronic; consequences; treatment control; personal control; perceived control; distress (depression and anxiety); intrusion; avoidance; and hyperarousal). Tabachnick & Fidell, (2007) propose that sufficient power is achieved with $N > 50 + 8m$ (m is the number of independent variables). This method suggests we need 130 patients.

Samples

All patients admitted to UKM Medical Centre with a provisional diagnosis of stroke were cross checked with the routinely collected stroke audit data. Potential participants will be identified with the help of the lead stroke clinician from inpatients and outpatients admission. Confirmation of stroke is via medical records. Potential participants will be approached by a letter from the lead clinician and given written information about the study. Those who fulfilled the inclusion and exclusion criteria from information gathered from medical notes or observation by the lead clinician will be invited by letter to take part and asked to return a reply form to indicate if they agree or not to participate in the study. If they decided to participate, they will be asked to sign a consent form in accordance with UKM ethical guidelines.

Inclusion criteria

Potential patients will be recruited once they have been confirmed with diagnosis of stroke with no severe aphasia, no alcohol dependency or evidence of substance abuse. Potential patients should also preserved cognitive function indicated by screening measure.

Exclusion criteria

Patients will be excluded from this study if they have been diagnosed having psychiatric history, inability to provide informed consent due to poor comprehension or communication and co-morbidity indicating difficult medical history.

Outcome

Primary and secondary outcome measures

Observer Assessed Disability (OAD) (Partridge, Johnston & Edwards, 1987) designed to assess functional limitation consists of 18 movements of activities. It is a performance assessment designed to measure activity limitation in stroke patients. A score of 1 is given for every completed activity, giving a possible score of 18.

Secondary outcome measure will be based on Barthel Index of Activities of Daily Living (Mahoney and Barthel, 1965). This is the measure of physical disability used widely in stroke research and routine clinical practice. It gives a score of 0 (complete physical dependency) to 20 (no physical dependency).

Psychological variables

Illness representations are assessed using Illness Perception Questionnaire-Psychometrically Shortened (IPQ-PS, Araujo-Soares, Weinman, Moss-Morris, & Sniehotta (in preparation). This is a self report questionnaire used for assessing seven (7) cognitive illness representations consisting of identity, consequences, causes, timeline acute, timeline chronic, treatment control and personal control. However in this study, the researcher will use only five (5) illness representations which consist of timeline acute; timeline chronic; consequences; treatment control; personal control to represent the illness representations.

Perceived Control will be assess using Recovery of Locus Control (RLOC, Partridge and Johnston, 1989). This is a self report questionnaire and was used as in the previous study with stroke patients (Partridge and Johnston, 1989). This scale has 9 items which are rated from strongly agree to strongly disagree. Five items are phrased in the direction of internal control (e.g. 'It is what I do to help myself that's really going to make all the difference'.) and 4 in the direction of external or chance (e.g. 'I have little or no control over my progress from now on').

Psychological Distress and Posttraumatic Stress Symptoms will be measured using Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983) and Impact of Event Scale-Revised (IES-R) (Weiss & Marmar, 1997). This is a measure of posttraumatic stress symptoms which is parallel with the Diagnostic Statistical Manual of Mental Disorder (DSM).

All the measures will be presented to the participants at both six weeks post stroke and again at six months post stroke.

Cognitive Screening

All stroke patients will be screened for their cognitive ability by using Addenbrooke's Cognitive Examination - Revised (ACE-R; Mioshi, Dawson, Mitchell, Arnold & Hodges, 2006). It is a cognitive test that contains 5 sub-scores, each representing one cognitive domain: attention/orientation (18 points), memory (26 points), verbal fluency (14 points), language (26 points) and visuospatial abilities (16 points). The total score is 100, higher scores indicate better cognitive functioning. Patients with a total score of less than 82 will be excluded from responding to further questionnaires. This measurement will be used to screen cognitive impairment at the beginning of each interview before they can proceed to the next pencil paper and also performance tasks.

Recovery from Physical Disability

We will replicate the method used by Johnston et al. (2007), and Johnston, Morrison, MacWalter and Partridge (1999) to measure recovery from disability. Observer Assessed Disability (OAD) and Barthel Index will be used to measure the degree of physical disability for this purpose. Johnston et al. (2007) defined recovery for their study as "the deviation from the statistically expected disability at 6 months from baseline, with scores greater than 0 indicating a better than average recovery (based on the performance of the total group)".

Procedure

The participants who agree to participate will be seen by the researcher to complete the test booklet on two occasions. The first occasion will be approximately six (6) weeks after the stroke and then again six (6) months after the stroke. The researcher will conduct different tasks including pencil and paper tasks and a performance task in which the researcher will ask the participant to perform various simple physical activities (Please refer to the method section.) Before participants are asked to answer the pencil and paper task, they will be screened for their cognitive ability by the researcher. Participants that are not cognitively impaired based on the cognitive screening test will be proceeding to the next tasks. If they are cognitively impaired they will be excluded from the study.

For patients that are not cognitively impaired they will proceed for the pencil and paper task. The researcher will read the questions to the participants and will provide the answer based on the questionnaires. This session will be audio recorded. However, for the physical task, the participants will be asked to perform some physical activities and will be observed by the researcher. To complete the entire block of tasks will take approximately an hour and a half of participants' time, although this can easily be interspaced with short breaks, if participants prefer.

Approaching Participants at 6 months after stroke

Participants Who have made consent to the study, will have to agree to the researcher's accessing their medical records. As such, in order to avoid any potential distress to family, the researcher will check the medical records, and with the administration personnel (who follow all patients for up to one year after discharge from hospital) before approaching for follow up to ensure that this is still appropriate.

Analyses

The primary analyses will assess the ability of predictors (illness representations, anxiety, depression, and posttraumatic stress symptoms) to predict recovery from disability controlling the demographic and clinical factors. To determine the predictors of recovery from disability, multiple regressions will be used. Correlations will be carried out to assess the relationship between different predictors (illness representations, anxiety and depression and posttraumatic stress disorder) and the outcome variables. General Linear Model Repeated measures will be used to assess changes in the way stroke patients think about their illness over time and the changes in their emotional state from 6 weeks to 6 months post-stroke.

DISCUSSION

There has been a wide range of research in medical field to look at pharmacological effects on immediate recovery after stroke. However, there is lack of research to investigate the contributions of other effects that influence recovery after stroke. Therefore, this research is important to carry out and examine the influence and contribution of psychological factors toward recovery. Knowledge of illness representations, perceived control, psychological distress and posttraumatic stress symptoms which are associated with post stroke cognitive and emotional distresses might provide clues to their causes, help patients with stroke to identify their ability to reduce physical disability, and be available to participate in socially. Therefore, in the future we can join the pharmacological (medical approach) and psychological factors and study the effect of recovery from physical disability following a stroke. In addition, an appropriate intervention could be developed to synchronize with this finding in the future.

Furthermore, there are no studies that have been done in Malaysia that looks at psychological variables in predicting disability among stroke survivors. This study was based on the model of well-established studies like Johnston, Morrison, MacWalter, Partridge (1999); Johnston, et al., (2007). In fact, this study will be the first kind in Malaysia, which will enhance further research focusing on the psychological variables in the reduction of physical disability following stroke. Hence, it will provide information to the healthcare services and the government to improve the services and treatment intervention of the stroke sufferers.

REFERENCES

- Araujo-Soares, V., Weinman, J., Moss-Morris, R., & Sniehotta, F.F. (in preparation). Measuring illness perceptions using a psychometrically shortened version of the IPQ-R the IPQ-PS.
- Aziz, N.A, and Raymond, A.A. (2008). Managing Further Rehabilitation in Longer-Term Stroke Patients in the Community: A New Approach. *Med & Health 3(1): 1-6*
- Bonita, R. Solomon, N., Broad, J.B. (1997). Prevalence of stroke and stroke-related disability: estimates from the Auckland stroke studies. *Stroke*. 28: 898-902.
- Bruggimann, L., Annoni, J. M., Staub, F., Von Steinbuchel, N., Van Der Linden, M., and Bogousslavsky, J. (2006). Chronic posttraumatic stress symptoms after nonsevere stroke. *Neurology*, 66(4), 513-516.
- Buckley, T.C., Green, B. L., and Schnurr, P.P. (2004). Trauma, PTSD and Physical Health, Clinical Issue Asseaaing Psychological Trauma and PTSD (2nd ed) Ed Wilson J.P and Keane, T.M. New York., 441-465.
- Caro J.J., Huybrechs K.F., and Dunclease J. (2000). Management patterns and cost of acute ischemic stroke ; an international study. *Stroke*31;582-590.
- Cochrane Database Systematic Review. (2005). Organised inpatient (stroke unit) care for stroke. Cochrane Stroke Group. Cochrane Database Systematic Review 2.
- de Fries F.L., Green L.W., Levine S. (2007). Health promotion and the compression of morbidity In Johnston, M., Bonetti, D., Joice, S., Pollard, B., Morrison, V., Francis, J.J., & MacWalter, R. (2007). Recovery from disability after stroke as a target for behavioural intervention: Results of a randomized controlled trail. *Disability and Rehabilitation; 29 (14) : pp. 1117-1127.*
- 25 (2011):11-21
- Dijkerman HC, Wood VA, Longton Hewer R. (1996) Long-term outcome after discharge from stroke rehabilitation unit. *J R Coll Physician Lond* 30: 538-546.
- Ezzat S.G., Asmawati, D., Yahaya, M., Raymond, A.A. (2011). Does stroke patients suffers from PTSS? *Jurnal Psikologi Malaysia*, 25(2011):11-21.
- Fisher, K., and Johnston, M. (1996). Experimental manipulation of perceived control and its effect on disability. *Psychology and Health; 11, 657-669.*
- Feigin V.L, Lawes C.M.M., Bennett D.A., Anderson C.S. (2003). Stroke epidemiologi : a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. *Lancet Neurology*, 2 : 43-53.
- Foulkes M.A., Wolf P.A., Price T.R., Mohn J.P., Heir D.B. (1988). The stroke data bank : design, methods, and baseline characteristics. *Stroke*. 19 : 547-554.
- Glamcevski II M.T. and Pierson, J. (2005). Prevalence of and Factors Associated with Poststroke Depression: A Malaysian Study. *Journal of Stroke and Cerebrovascular Diseases, Volume 14, Issue 4, July-August 2005, Pages 157-161*
- Green , B. L., Rowland, J.H., Krupnick, J.L., Epstein, S.A., Stockton, P., Stern, N.M., et al. (1998). Prevalence of posttraumatic stress disorder in women with breast cancer. *Psychosomatics*, 39, 102-11
- Hagger, M.S. and Orbell, S. (2006). Illness representations and emotion in people with abnormal screening results. *Psychology and Health, Vol 21(2) : 183-209*

- Hamidon, B.B., and Raymond, A.A. (2003). Risk factors and complications of acute ischaemic stroke patients at Hospital Universiti Kebangsaan Malaysia (HUKM) *Med J Malaysia*. Oct;58(4):499-505.
- House, A. (1987) Mood disorder after stroke : A review of the evidence. *International Journal of Geriatric Psychiatry*, 2, 211-221.
- Jamrozik K., Broadhurst R.J., Lai N., Hankey G.J., Burvill P.W. & Anderson C.S. (1999). Trends in the incidence, severity, and short-term outcome of stroke in Perth, Western Australia. *Stroke*; 30: 2105-2111.
- Jaya, F., Nyunt Win, M., Abdullah M.R., Abdullah, M.R., Abdullah, J.M. (2002). Stroke Patterns in Northeast Malaysia: A Hospital-Based Prospective Study *Neuroepidemiology* 2002;21:28-35
- Johnston, M., Morrison, V., MacWalter, R.S., Partridge, C.J. (1999). Perceived control, coping and recovery from disability following stroke. *Psychol Health*; pp. 181-192.
- Johnston, M., Bonetti, D., and Pollard, B. (2002). Disability as behaviour: Models of measurement and explanation. In: Backman L, von Hofson C, editors, *Psychology at the turn of the millennium*, Vol. 1: Cognitive, biological and health perspectives. Oxford; Elsevier; 2002, pp. 3704-3710.
- Johnston, M., Bonetti, D., Joice, S., Pollard, B., Morrison, V., Francis, J.J., and MacWalter, R. (2007). Recovery from disability after stroke as a target for behavioural intervention: Results of a randomized controlled trial. *Disability and Rehabilitation*; 29 (14) : pp. 1117-1127.
- Kaplan R.M. (2000). Behaviour as the central outcome in health care. *Am Psychologist*; 45; 1211-1220.
- Mahoney F. J., and Barthel D.W. (1965) Functional evaluation : The Barthel Index. *Maryland State Medical Journal*; 14;14:61-65
- Mayo, N., Wood-Dauphinnee, S., Cote, R., Gayton, D., Carlton, J., Buttery, J., Tamblyn, R. (2000). There's no place like home: An evaluation of early supported discharge for stroke. *Stroke*; 31(5); 1016-1023.
- Merriman C., Norman P., and Barton, J. (2007). Psychological correlates of PTSD symptoms following stroke. *Psychology, Health & Medicine*, 12:5, 592-602.
- Ministry of Health. 2008 Health Indicator. MOH
- Mioshi, E., Dawson, K., Mitchell, J., Arnold, R., and Hodges, J.R. (2006). The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. *Int. J. Geriatr Psychiatry*; 21: pp. 1078-1085.
- Morrison V, Pollard B, Johnston M, MacWalter R. (2005) Depression and anxiety following stroke : Demographic, clinical and psychological predictors of 3 years outcome. *J. Psychosomatic Research*; 59;209-213.
- Murray C.L., Lopez A.D. (1997). Mortality by cause of eight regions of the world global burden of disease study. *Lancet* . 348: 1269-1276.
- Niemi, M.L., Lauksonen, R., Kotila, M., Waltimo, O. (1988). Quality of life 4 years after stroke. *Stroke*, 19 : 1101-1107.
- Ong, T Z and Raymond A. A. (2002). Risk Factors for Stroke and Predictors of One-Month
- Partridge C, Johnston M, Edward S. (1987) Recovery from physical disability following stroke : Normal patterns as a basis for evaluation. *Lancet*; 272-2.
- Pollard, B., and Johnston, M. (2001). Problem with the Sickness Impact Profile: a theoretically based analysis and a proposal for a new method of implementation and scoring. *Social Science and Medicine*; 52; pp 921-934.
- Rameezan, B.A, Zaliha, O. (2005). Functional status of acute stroke patients in University Malaya Medical Centre (UMMC), Kuala Lumpur, Malaysia. *Med J Malaysia*. Dec;60(5):548-59.
- Sampson, M.J., Kinderman, P., Watts, S., and Sembi. S. (2003). Psychopathology and autobiographical memory in stroke and non-stroke hospitalized patients. *Int. J. Geriatr Psychiatry*; 18: pp. 23-32.
- Sembi, S., Tarrier, N., O'Neill, P., Burns, A., and Faragher, B. (1998). Does post-traumatic stress disorder occur after stroke: A preliminary study. *International Journal of Geriatric Psychiatry*, 13(5), 315-322.
- Siti Aminah, O., Normah, C. D., and Ponnusamy, S. (2008). Factors influencing cognitive impairment among stroke patients. *Proceedings Simposium Sains Kesihatan Kebangsaan ke 7, 18 – 19 Jun: 226 – 229*.
- Sulaiman, A.H., Zainal, N.Z., Tan, K.S., Tan, C.T. (2002). Prevalence and associations of post-stroke depression. *Neurol j southeast asia vol 7 : 71 – 75*
- Sloan, E.P. (2005). The neurological exam in the Emergency Department: A focus on stroke and ICH patients. Foundation for Education and Research in Neurological Emergency.
- Tabachnick, B.G., and Fidell, L.S. (2007). *Using Multivariate Statistics* (5th ed). (pp. 123). New York, Pearson.
- Wade D.T., and Longton-Hewer, R. (1987). Functional abilities after stroke : Measurement, natural history and prognosis. *Journal of Neurology, Neurosurgery and Psychiatry*, 50, 177-182.
- Warlow C.P. (2001). *Stroke: A practical guide to management*, 2nd ed, Oxford: Blackwell Science.
- Wilcox, V.L., & Kasl, S.V., and Berkman, L.F. (1994). Social support and physical disability in people after hospitalization : A prospective study. *Health Psychology*, 13, 170-179.

- World Health Organisation. (1980). *The International Classification of Functioning Disabilities and Handicap*. Geneva.
- World Health Organization. (2000). *The world health report 2000*. Geneva.
- World Health Organization. (2001). *International Classification of Functioning Disability and Health : ICF*. Geneva, Switzerland: Author.
- World Health Organization. *World Health Statistics*. (2007). *Future health: Projected deaths for selected causes to 2030*. *The World Health Report, WHO (2007)*. pp. 12.
- Zigmond A.S, Snaith, R.P. (1983). *The Hospital Anxiety and Depression Scale*. *Acta Psychiat Scand* 1983; 67:361-370.