INTRODUCTION

Among those patients who survive stroke, sleep disorders (SDs) are common problems.

Sleep is a complex process involving the interaction of several cerebral regions. Certain structures have key-roles in sleep regulation, particularly the brain stem, the thalamus and the anterior basal brain regions ***(Mahowald, 2000).***

Any condition which leads to brain cell damage or neurotransmitter dysfunction is thus susceptible to influence the functioning of cerebral structures or inter-connections between structures responsible for regulating sleep-wake processes. Stroke, either ischemic or hemorrhagic is one of these conditions which affect these areas of brain responsible for sleep regulation ***(Bassetti, 2005).***

A large percentage of stroke patients ranging from 20% up to 63% experience sleep disorders (SDs) ***(Bassetti, 2005).*** This may include sleep disordered breathing (SDB) like sleep apnea (SA), habitual snoring and Cheyne-Stokes respiration (CSR). Also, sleep-wake disorders like insomnia, hypersomnia; excessive daytime sleepiness (EDS), parasomnia, circadian rhythm disorder, and sleep-related movement disorder such as restless legs syndrome (RLS) and periodic limb movement disorder (PLMD) ***(Wallace et al., 2011).***

Furthermore, the consequences of untreated sleep disorders may impede stroke rehabilitation, lengthen hospital stay and influence stroke outcomes and stroke recurrence ***(Culebras, 2009).***

It is further noted that particular sites of lesion may give rise to predictable deficits of sleep. Pontine strokes, for example, may be expected to affect REM sleep either unilaterally or bilaterally, or destroy REM atonia to give rise to REM behavior disorders ***(Bassetti, 2005).***

Obstructive sleep apnea (OSA) has been found in as many as 60% of stroke patients in the post-acute period ***(Disler et al., 2002).*** Also, sleep-disordered breathing precedes stroke and may thus play an important role in its development ***(Arzt et al., 2005).***

Excessive daytime sleepiness due to (OSA) has major impacts on patient's capacity to engage in their rehabilitation efforts. In fact, research has shown that the recovery and functional outcome of stroke survivors is compromised when they suffer from sleep-disordered breathing (SDB) ***(Cherkassky et al., 2003).***

AIM OF THE WORK

- Description of prevalence of sleep disorders in patients who survived stroke.
- Description of severity of sleep disorders after stroke.
- Making correlation studies between sleep disorders after stroke and stroke demographic, clinical and risk factor variables.

INTRODUCTION TO STROKE

Definition

Stroke is defined as a rapidly developing clinical signs of neurological deficit as focal rather than global disturbance of cerebral functions with symptoms lasting more than 24 hours or leading to death before 24 hours with no apparent cause after adequate investigations other than vascular origin ***(Roger et al., 2011).***

Epidemiology

Around fifteen million people across the world suffer from stroke each year. Among these, five million die and another five million are permanently disabled. Four out of five strokes occur in low- and middle- income countries which can least afford to manage the consequences of this disease ***(Lopez et al., 2006).*** Stroke is the second leading cause of death in the western world after heart disease and before cancer. Also, it causes 10% of deaths worldwide ***(World Health Report, 2004).***

In Egypt, the overall prevalence rate of stroke is high with a crude prevalence rate of 963\100.000 inhabitants ***(Abd-Allah and Moustafa, 2014).***

In another study aiming to find lifetime prevalence of stroke in upper Egypt, the total lifetime prevalence of stroke was 8.5\1,000 in the population aged 20 years and more. It

increased with advancing age and was higher among males than female among all age groups except in the childbearing period (20 years to less than 40 years of age). Lifetime prevalence of ischemic stroke (7.2\1,000) was higher than hemorrhagic stroke (1.1\1,000) ***(El-Tallawy et al., 2015).***

Classification

Stroke is classified into two main categories; ischemic and hemorrhagic. About 85% of all first ever strokes are ischemic, 10% primary intarcerebral hemorrhage (ICH) and 5% subarachnoid hemorrhage (SAH). For ischemic stroke, 25% are large artery disease, 25% small artery disease, 20% cardiac embolism, 5% other causes and 25% of undetermined etiology ***(Donnan et al., 2008)***.

1. Ischemic stroke

It occurs when blood supply to a part of brain decreased causing brain tissue dysfunction at that area. This is usually due to thrombosis, embolism, systemic hypoperfusion or venous thrombosis ***(Guercini et al., 2008).*** According to location, there is total anterior circulation, partial anterior circulation, lacunar or posterior circulation stroke ***(Rothwell, 2009).***

A- Thrombotic stroke

It occurs when a thrombus forms around atherosclerotic plaques. It may be arterial or venous. A thrombus itself can

break off and cause embolic stroke. According to vessels the thrombus form in, two types of pathology are seen; large vessel and small vessel disease ***(Hill, 2005).***

B- Embolic stroke

It occurs when an embolus occludes an artery. Embolus may be a thrombus, a travelling particle or debris in an arterial blood stream. It also may other substances such as fat, air, cancer cells or clumps of bacteria ***(Ay et al., 2005).***

2. Hemorrhagic stroke

Intracerebral hemorrhage may occur spontaneously due to a hypertensive disease, coagulation disorders, vascular malformations and diet ***(Ma et al., 2011)***. Cortical hemorrhage occurs due to amyloid angiopathy which is a consequence of hypertension and it becomes increasingly frequent as populations become older ***(Fan et al., 2011).***

3. Subarachnoid hemorrhage (SAH):

It occurs usually due to rupture of aneurysms in the brain. It may cause symptoms in accordance with stroke definitions, so it should be regarded as a stroke ***(Bernardini and Deshaies, 2001).***

According to the etiology, stroke can be further subdivided into many types as illustrated at Table 1.

Table (1): Stroke subtypes ***(Amarenco et al., 2009).***

1. Ischemic
1.1. Atherothrombotic
1.1.1. Extracranial
1.1.2. Intracranial
1.2. Small vessel disease (sporadic)
1.3. Cardiac emboli
1.4. Other causes
1.4.1. Dissection
1.4.2. Rare or hereditary large- or medium-sized artery disease (e.g. moya-moya disease, fibromuscular dysplasia)
1.4.3. Rare or hereditary small vessel disease
1.4.4. Coagulopathy
1.4.5. Metabolic disease with arteriopathy
1.4.6. Vasculitis
1.4.7. Other rare entities
1.5. Coexisting causes
1.6. Unknown
1.7. Unclassifiable
2. Hemorrhagic
2.1. Hypertension-related small vessel disease (hemorrhagic type)
2.2. Cerebral amyloid angiopathy
2.2.1. Sporadic
2.2.2. Hereditary
2.3. Bleeding diathesis
2.3.1. Drugs that decrease clotting
2.3.2. Other hemostatic or hematologic disorders
2.4. Vascular malformation
2.4.1. Arteriovenous malformation
2.4.2. Dural fistula
2.4.3. Ruptured aneurysm
2.4.4. Cavernoma
2.4.4.1. Sporadic
2.4.4.2. Familial
2.5. Other causes
2.5.1. Tumor related
2.5.2. Toxic (e.g. sympathomimetic drugs, cocaine)
2.5.3. Trauma
2.5.4. Arteritis, angiitis, endocarditis (ruptured mycotic aneurysm), infections
2.5.5. Rare entities (e.g. dissection of intracranial arteries)
2.6. Coexisting cause
2.7. Unknown
2.8. Unclassifiable
3. Subarachnoid hemorrhage
3.1. With aneurysm
3.2. With dissection
3.3. Traumatic
3.4. Neoplastic (melanoma)
3.5. Unknown
4. Cerebral venous thrombosis
5. Spinal cord stroke
5.1. Ischemic
5.2. Hemorrhagic
5.2.1. Associated with arteriovenous malformation
5.2.2. Associated with coagulopathy

Stroke risk factors

They can be divided into modifiable and non-modifiable risk factors. Modifiable risk factors are hypertension, atrial fibrillation, high lipid levels, lack of activity, obesity, diabetes mellitus, smoking and heavy alcohol consumption ***(American heart association, 2007).*** Non-modifiable risk factors are age, sex, ethnicity and hereditary factors.

A- Modifiable risk factors:

1. Hypertension:

Hypertension accounts for 35-50% of stroke risks factors ***(Whisnant, 1996)***. Reduction of blood pressure has been conclusively shown to prevent both ischemic and hemorrhagic stroke ***(Psaty et al., 2003).***

2. Atrial fibrillation (AF):

Atrial Fibrillation (AF) patients have a risk of 5% to develop stroke, each year. This risk is higher for those who have valvular A.F ***(Wolf et al., 2011).***

3. Blood lipids:

High blood cholesterol levels and increased some serum lipoproteins have been associated with ischemic stroke. Also, cholesterol level lowering does seem to reduce stroke risk ***(O'Regan et al., 2008).***

4. Diabetes mellitus (DM):

Diabetic patients are 2 or 3 more likely to develop stroke. They usually have hypertension and hyperlipidemia. It was also seen that disease control reduces microvascular complications such as retinopathy but not macrovascular complications such as stroke ***(Dormandy et al., 2005)***.

5. Smoking:

It is a strong independent risk factor for ischemic stroke ***(Murat and Erturk, 2012)***. Smoking causes vasoconstriction which may further narrow the stenoses of intracranial arteries and cause stroke ***(Kool et al., 2012).***

6. Obesity:

There is a correlation between abdominal obesity and ischemic stroke ***(Ohira et al., 2009).*** It was found that there is a linear association between body mass index (BMI) and ischemic stroke. Hypertension, hyperlipidemia and hyperglycemia attenuate this correlation suggesting that obesity is mediated by other risk factors of stroke ***(Wilson et al., 2011).***

7. Alcohol Consumption:

The relationship between alcohol consumption and ischemic stroke follows a J-shaped curve ***(Reynold et al., 2003).***

B-Non-modifiable risk factors

1. Age

It is a very strong risk factor for every type of stroke. Stroke in people aged 75-84 years is about 25 times more common than those who aged between 45-54 years old ***(Bamford et al., 1990).*** 95% of strokes occur in people aged 45 years or older. Two thirds occur in people over 65years old age. Mortality also increases with age ***(Senelick et al., 2009).***

2. Sex

Males are 1.25 times more likely to suffer strokes than females, but 60% of deaths from strokes occur in females ***(Villarosa et al., 1993).***

Some risk factors exclusively affect females such as pregnancy, child-birth, menopause and hormonal replacement therapy ***(National institute of Neurological disorders and stroke NINDS, 1999).***

3. Ethnicity and heredity

Stroke is more common in people whose relatives suffered stroke. This indicates certain genetic predispositions for developing stroke. For example, there is an association between Apo-E gene and ischemic stroke ***(Fan, 2011).***

Ischemic stroke pathophysiology:

In thrombotic strokes, atherosclerosis may disrupt blood supply by narrowing blood vessels and causing blood clots or by releasing showers of small emboli due to disintegration of the atherosclerotic plaque ***(Straus et al., 2002).*** On the other hand, embolic infarction occurs due to emboli from heart after atrial fibrillation or carotids. They break off, enter cerebral circulation and lodge in and occlude cerebral vessels ***(Goldstein et al., 2006).***

Due to collateral circulation, there is a spectrum of severity. Some tissues die, others are injured and could potentially recover. The recoverable area is the ischemic penumbra ***(O'Regan et al., 2008).***

In the ischemic area, oxygen and glucose become depleted. Production of adenosine triphosphate (ATP) fails, leading to failure of energy dependent processes necessary for tissue survival. This sets off a series of events that result in cellular injury and death ***(Halkes et al., 2006).***

Also, a major cause of neuronal injury is release of the exictatory neurotransmitter, glutamate. Normally, it is kept at low concentration outside the cell, guided mainly by conentration gradients of ions, mainly Na+, across cell membrane ***(Bartolucci and Howard, 2006).***

Ischemia induces production of free radicals that react and damage cellular and extracellular elements. Brain tissue is

vulnerable to ischemia since it has little respiratory reserve and is completely dependent on aerobic metabolism, unlike most other organs ***(Lutsep et al., 2008).***

Ischemia, also causes loss of structrual integrity of brain tissue and blood vessels, partly through release of matrix metalloproteases, which are zinc and calcium dependent enzymes that break down collagen, hyaluronic acid and other connective tissue. The loss of vascular structural integrity results in a breakdown of the protective blood brain barrier that contributes to cerebral edema, which can cause secondary progression of the brain injury ***(Den Hertog et al., 2009).*** Many mechanisms involved in stroke pathophysiology are illustrated at Figure 1.

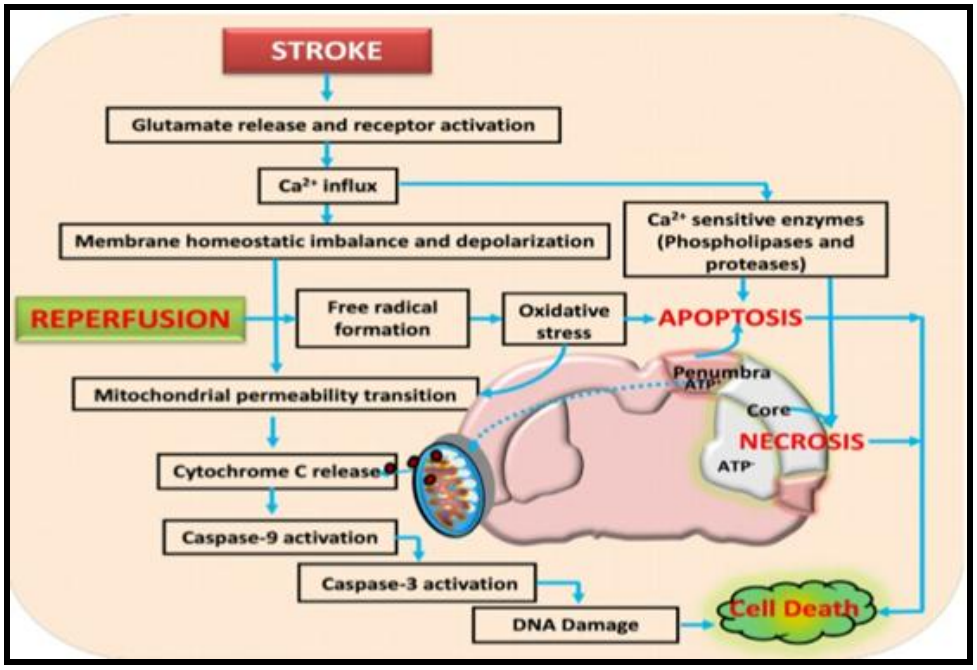

Figure (1): Ischemic stroke pathophysiology ***(Metha and Vemuganti, 2014).***

SLEEP PHYSIOLOGY

Sleep Definition

It is a state of reduced awareness and responsiveness both to internal and external stimuli. This reduced awareness is, however, selective ***(Velluti, 2007).***

Sleep was thought to be a passive state that was initiated through withdrawal of sensory input. It is now believed that withdrawal of sensory awareness is a factor in sleep, but an active initiation mechanism that facilitates brain withdrawal is recognized ***(Siegel, 2005).***

It is different from coma, which is a state of unconsciousness in which a person fails to respond normally to painful stimuli, light or sound, lacks a normal walk-sleep cycle and does not initiate voluntary actions ***(Weyhenmyeye et al., 2007).***

Sleep Architecture

Since 1950s, there were two main states of sleep, non-rapid eye movement (NREM sleep) and rapid eye movement (REM sleep) ***(Terzano et al., 2010).*** The two states are heterogeneous and at any moment. They and wakefulness may not be as distinct as has previously been thought ***(Sheerson, 2005).*** Parts of brain may be in REM sleep where another part may be tending towards NREM sleep ***(Benloucif et al., 2008).***

The lighter stages of NREM sleep appear first alternating with brief episodes of wakefulness before deeper stages of NREM sleep are entered. NREM sleep, particularly its deeper stages predominates early in the night, while REM sleep appears at around 90 minutes intervals ***(Groeger et al., 2009).*** There are 4 to 6 of sleep cycles per night and as night progresses, REM episodes become longer and NREM sleep becomes shorter and lighter. Brief arousals to wakefulness are a normal feature of sleep ***(Groeger et al., 2009).***

Electrophysiology of Sleep

Wakefulness

In active wakefulness where person is awake and pursuing normal activities, EEG is characterized with dominant low amplitude, high frequency beta activity of 16-25 Hz. Muscle tone is usually high with high to moderate EMG activity and EOG readings exhibit REMs ***(Schupp et al., 2003)***, while in relaxed wakefulness, a person is awake but eyes are closed, EEG is characterized by a pattern of alpha waves with a frequency of 8-12 Hz and an amplitude of 20-40 microvolts. EOG readings show slow rolling movements at the transition to NREM. EMG readings show reduced amplitudes ***(Timothy et al., 2001).***

Non-Rapid Eye Movement Sleep (NREM Sleep)

**** Stage 1:***

In stage 1 of NREM, alpha rhythm 8-13 Hz which is characteristic of wakefulness diminishes to less than 50% and a mixture of slower theta 4-7 Hz and beta greater than 13 Hz appears. Slow, rolling eye movements may be noticed at this time. Vertex sharp waves begin to appear towards end of this stage. Involuntary muscle clonus occurs frequently resulting in jerky movement (hypnic jerks). EMG activity is moderate to low. It lasts from 5 to 10 minutes, where minor auditory stimuli will cause arousal ***(Chokroverty, 2007).***

**** Stage 2:***

It begins about 10-12 minutes after stage 1. It is characterized by sleep spindles 14-16 Hz and K complexes intermixed with vertex sharp waves. The background rhythm is a mixture of theta and delta waves less than 4 Hz composing less than 20% of the epoch ***(Siegel, 2005).*** EMG is low to moderate. It continues 10-20 minutes in the 1 – 2 cycles but predominates in later cycles. It is the most abundant sleep stage in the adults accounting for up to 50% of total sleep time (TST) ***(Schupp et al., 2003).***

**** Stage 3:***

It is called deep sleep, slow-wave sleep (SWS) which constitutes about15-25% of total sleep in adults. The sleeper is