INTRODUCTION

Migraine is one of the head complaints arousing the most interest in the scientific community in recent years. There has been great interest in its relationship with ischemic event as a vascular risk factor or the presence of clinically silent stroke in patients with migraine or stroke as a direct complication of migraine with aura. This new approach in previously existing & known problems has reopened the debate in the role of blood vessels in pathophysiology of migraine ***(Scher et al., 2005).***

Migraine is commonly described as a severe headache that is unilateral in location, throbbing in nature, and associated with nausea or photo and phonophobia or both. However, it is important to keep in mind that to satisfy an ICHD diagnosis of migraine, only 2 of the 4 ICHD criteria Care required **(Table 1)**. Thus, migraine headaches may be mild or even bilateral in location and still fulfill migraine criteria ***(Peterlin et al., 2008).***

Migraine has been considered for decades as an episodic disorder that has different types, including complicated cases. However, over the past 30 years several studies have been carried out looking at and delivering arguments for a possible association between migraine and brain changes. For this association, three lines of evidence can be recognized ***(Guercini et al., 2008).***

Migraine and stroke are associated with a higher frequency than expected when observing the prevalence of both

diseases among the general population. This relationship may be one of coincidence, similarity (migraine resembling stroke or stroke resembling migraine), origin (migraine and stroke as manifestations of the same underlying process) and causality (migraine may act as an additional risk factor for stroke or may be the direct cause of stroke) ***(Schwaag et al., 2003).***

Migraine can modify the homeostatic properties of the endothelium, favoring prothrombotic, pro-inflammatory and proliferative condition that predisposes towards atherogenesis and the development of thrombotic events other than migraine. Endothelial dysfunction is the result of (a) a reduction in the bioavailability of vasodilator substances (nitric oxide, for example) and an increase in contractile factors derived from the endothelium, causing an alteration in vascular reactivity (including the microvasculature), and (b) oxidative stress, which in turn promotes inflammatory processes ***(Ciancarelli et al., 2003).***

The most likely etiologic mechanism of posterior circulation territory infarcts in migraine patients seems to be hypoperfusion and/or embolism, rather than atherosclerosis or small vessel disease. During and after migraine attacks, sluggish low cerebral flow below an ischemic threshold has been described. A decrease in brain perfusion pressure (*e.g.* during migraine) theoretically affects the clearance and destination of embolic particles; narrowing of the arterial lumen and endothelial abnormalities stimulate formation of thrombi; occlusive thrombi further reduce blood flow and brain perfusion ***(Hennerici et al., 1998).***

Aim of the Work

To highlight the relationship between migraine, deep white matter (WM) lesions and posterior circulation ischemic cerebrovascular stroke.

Epidemiology, Prevalence & Incidence

Headache is a common condition that has affected humankind throughout history, with documented describtions in Egypt. However, it was not until 1988 that the first edition of the International Classification of Headache Disorder (ICHD) was published. Today, there are approximately 200 different headache disorders described in the ICHD second edition ***(Cutrer et al., 2014)***. The publication of the ICHD provided an operational tool that allowed greater uniformity in headache diagnoses and facilitated great strides in headache research and our understanding of headache disorders ***(Diamond & Franklin, 2005).***

Headache is defined as a pain arising from the head or upper neck of the body. The pain originates from the tissues and structures that surround the brain because the brain itself has no nerves that give rise to the sensation of pain (pain fibers). The periosteum that surrounds bones; muscles that encase the skull, sinuses, eyes, and ears; and meninges that cover the surface of the brain and spinal cord, arteries, veins, and nerves, all can become inflamed or irritated to cause the pain of a headache. This pain may be a dull ache, sharp, throbbing, constant, mild, or intense ***(Digre et al., 2011).***

In 2005, the International Headache Society released its classification system for headache. Because so many people suffer from headaches and because treatment sometimes is difficult, it was hoped that the new classification system would help health care professionals make a specific diagnosis as to the type of headache and allow better and more effective options for treatment.

There are three major categories of headache based upon the source of the pain:

- Primary headaches;
- Secondary headaches; and
- Cranial neuralgias, facial pain, and other headaches. ***(Garza et al., 2005).***

Migraine headaches are the second most common type of primary headache. Migraine headaches affect children as well as adults. Before puberty, boys and girls are affected equally by migraine headaches, but after puberty, more women than men are affected. **Table 1** demonstrates international classification of headache (ICHD-II) ***(Cutrer et al., 2014).***

Table (1): CHD-II migraine criteria.

A. At least 5 attacks fulfilling criteria B-D
B. Headache attacks lasting 4-72 hours(untreated or unsuccessfully treated)
C. Headache has at least two of the following characteristics:
1. Unilateral location
2. Moderate or severe pain intensity
3. Aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
4. Pulsating, pounding, or throbbing quality
D. During headache at least one of the following:
1. Nausea and/or vomiting
2. photophobia and phonophobia
E. Not attributed to another disorder

(Cutrer et al., 2014)

There are several types of migraine, all share basic features, and each person will suffer this headache in a unique way. Generally, however, migraine often begins as a dull ache and then develops into a constant, throbbing and pulsating pain that you may feel at the temples, as well as the front or back of one side of the head. The pain is usually accompanied by nausea and vomiting, and sensitivity to light and noise ***(Katsarava et al., 2014).***

The two most prevalent types of migraine are migraine with aura (formerly referred to as classic migraine) and migraine without aura (formerly referred to as common migraine) ***(Buse et al., 2014).***

Migraine without Aura

Migraine is a vascular headache, which means the headache is associated with changes in the size of the arteries inside and around the skull. During the pre-headache phase, blood vessels constrict; when vascular dilation occurs, the migraine begins. The blood vessels are thought to become inflamed as well as swollen, and it is believed that migraine pain is caused by this inflammation, as well as by the pressure on the swollen walls of the blood vessels ***(Bigal et al., 2008).***

Most migraine sufferers experience two to four headaches per month; but, some people can get one every few days, and others may only have one or two a year. Most migraine headaches last at least four hours, although very severe ones can last up to a week. Headaches may begin at any time of the day or night; and while a sufferer may wake up with one, a migraine will rarely awaken a person from sleep ***(Munakata et al., 2009).***

Approximately one-third of migraine sufferers experience an aura prior to the headache pain ***(Munakata et al., 2009).***

Migraine with Aura

While most migraine sufferers experience visual problems during the headache, you may be someone whose migraine begins with an aura, a manifestation of neurological symptoms. Generally, the aura begins from five to thirty minutes before the actual onset of the headache. You may see wavy or jagged lines, dots or flashing lights; or, you experience

tunnel vision or blind spots in one or both eyes. The aura can include vision or hearing hallucinations and disruptions in smell (such as strange odors), taste or touch. It can become even more disconcerting or frightening if it involves feelings of numbness, a "pins-and-needles" sensation or even difficulty in recalling or speaking the correct word. These neurological events may last sixty minutes and will fade as the headache begins ***(Lewis et al., 2004).***

Hemiplegic Migraine

If you suffer from this rare but severe type of migraine with aura, you probably also have a family history of it. The hemiplegic migraine often begins with temporary motor paralysis and/or sensory disturbances on one side of the body, followed by the headache -- within the hour -- which may be accompanied by numbness or the "pins and needles" sensation. When the headache appears, the initial neurological symptoms may disappear ***(Naumann et al., 2008).***

Ophthalmoplegic Migraine

Also a rare and severe migraine, the ophthalmoplegic migraine's pain usually surrounds the eyeball and lasts from a few days to a few months. There may be paralysis in the muscles surrounding the eye. If these symptoms occur, you should seek immediate medical attention because the symptoms can be caused by pressure on the nerves behind the eye ***(Nestoriuc et al., 2008).***

Retinal Migraine

Another rare migraine, the retinal type starts with a temporary, partial, or complete loss of vision in one eye. It is followed by a dull ache behind that eye that may spread to the rest of the head ***(Pringsheim et al., 2008).***

Basilar Artery Migraine

This very rare form of migraine is accompanied by dizziness, confusion or lack of balance. It comes on suddenly and can result in fleeting visual disturbances, the inability to speak properly, ringing in the ears, and vomiting. Throbbing occurs in the back of the head. The basilar artery migraine is strongly related to hormonal influences and primarily strikes young adult women and adolescent girls; as sufferers age, the migraine with aura may replace the basilar artery type ***(Lipton et al., 2007).***

Abdominal Migraine

It is difficult to diagnose this migraine because the pain is felt in the abdomen. Nausea, vomiting and diarrhea may occur, and the pain usually occurs in the middle of the abdomen. The attack typically lasts hours and occurs mostly in children as a forerunner of migraine ***(Sierpina et al., 2007).***

Though they share a common name, migraines and chronic migraines (CM) are two different conditions. Many people with migraines will never develop CM headaches, but having migraines increases your risk for developing the chronic condition later ***(Goadsby et al., 2007).***

A migraine headache is also called an episodic migraine (EM). An EM occurs occasionally. People who experience EM headaches can go weeks and months between migraine attacks. People with CM, however, experience migraines 15 or more days in a month ***(Schürks et al., 2009).***

Chronic migraine is a distinct and relatively recently defined sub-type of Chronic Daily Headache. The International Headache Society defines chronic migraine as more than fifteen headache days per month over a three month period of which more than eight are migrainous, in the absence of medication over use. Episodic migraine is the other migraine sub-type, which is defined as less than 15 headache days per month ***(Grazzi et al., 2010 "a").***

CM is associated with a wide range of psychiatric and somatic comorbidities, more so than EM. Up to 25 % of migraineurs meet criteria (**table 2**). In the American Migraine Prevalence and Prevention (AMPP) study, CM patients were almost twice as likely as EM patients to meet the criteria for depression, and similar results were seen in the International Burden of Migraine Study (IBMS). A similar distinction between EM and CM is seen with respect to anxiety disorders. It has also been suggested that posttraumatic stress disorder occurs at a significantly higher rate in persons with CM than in EM, which may be explained in a subgroup of patients by childhood maltreatment. CM patients tend to have a higher Body Mass Index than EM patients, and around 25 % of CM patients are obese. CM patients suffer more than twice as

frequent (around 30 % of patients) from chronic non-headache pain disorders as compared to EM patients. Respiratory disorders and cardiac risk factors—including hypertension, diabetes mellitus and high cholesterol—were also significantly more reported by CM patients in the AMPP. CM patients are less likely to be full-time employed and are more likely to be occupationally disabled ***(Tepper et al., 2004).***

Table (2): ICHD-III beta criteria for chronic migraine

A. Headache (tension-type-like and/or migraine-like) on C15 days per month for 3 months
B. Occurring in a patient who has had at least five attacks fulfilling criteria for migraine without aura and/or migraine with aura
C. On C8 days per month for[3 months, fulfilling any of the following:
Criteria for migraine without aura
Criteria for migraine with aura
Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative
D. Not better accounted for by another ICHD-3 diagnosis

(Tepper et al., 2004)

The impact of chronic migraine can be very disabling. Being incapacitated for over half the month sometimes means that people are unable to work at all, with some claiming disability living allowance. Unfortunately, in many cases, current therapies are not enough to prevent or reduce the impact that chronic migraine has on people's lives. This can lead to sufferers frequently becoming depressed and unable to cope. ***(Grazzi et al., 2010 "b").***

Just like episodic migraine there is no single cause for chronic migraine. Some people find that they have defined triggers such as caffeine, bright lights, hormone, food or sleep deprivation. However for some people there is a steady progression in headache frequency, especially in long term sufferers. This can lead to the migraines becoming so frequent that they cross the threshold of more than 15 days per month and become defined as chronic migraine ***(Kurth et al., 2009).***

Primary headaches can affect the quality of life. Some people have occasional headaches that resolve quickly while others are debilitated. While these headaches are not life-threatening, they may be associated with symptoms that can mimic strokes ***(Leroux & Ducros, 2008).***

The exact causes of migraines are unknown. A popular theory is that various triggers cause abnormal brain activity, which in turn causes changes in the blood vessels in the brain. This is called the neurovascular theory. Genetics plays a role in migraines and there are some forms of migraines that are associated with inherited abnormalities in certain parts of the brain. Migraine pain is moderate to severe, often described as pounding, throbbing pain. Migraine headaches can last from four hours to three days and usually occur one to four times per month. Migraines are associated with symptoms such as sensitivity to light, noise, or odors; nausea or vomiting; loss of appetite; and stomach upset or abdominal pain. When a child is having a migraine, he or she often looks pale, feels dizzy, has

blurred vision, fever, stomach upset, along with the symptoms listed above ***(Edlow et al., 2008).***

A small percentage of children's migraines include recurrent (cyclic) gastrointestinal symptoms, vomiting being the most common. Cyclic vomiting means that the symptoms occur on a regular basis -- about once a month. These types of migraines are sometimes called abdominal migraines ***(Bajwa & Sabahat, 2014).***

Pathogenesis

Migraine is a form of sensory processing disturbance with wide ramifications for central nervous system function, and while pain is used as the exemplar symptom, a brain-centered explanation provides a framework to understand all the manifestations of migraine. ***(Etminan et al., 2005)***

Genetics of migraine

One of the most important aspects of the pathophysiology of migraine is the inherited nature of the disorder. It is clear from clinical practice that many patients have first-degree relatives who also suffer from migraine. Transmission of migraine from parents to children has been reported as early as the seventeenth century, and numerous published studies have reported a positive family history ***(Stam et al., 2009).***

Genetic epidemiology

Studies of twin pairs are the classical method to investigate the relative importance of genetic and environmental factors. A Danish study included 1,013 monozygotic and 1,667 dizygotic twin pairs of the same gender, obtained from a population-based twin register. The pairwise concordance rate was significantly higher among monozygotic than among dizygotic twin pairs ($P<0.05$). Several studies have attempted to analyze the possible mode of inheritance in migraine families, and conflicting results have been obtained. Both twin studies and population-based epidemiological surveys strongly suggest that migraine without aura is a multifactorial disorder, caused by a combination of genetic and environmental factors ***(Tietjen et al., 2009)***.

An unexplained but epidemiologically well-established predisposition relates to methyltetrahydrofolate reductase gene mutation C677T that is certainly overrepresented in migraine with aura. The presence of aura seems to be associated, in rarer inherited cases, such as CADASIL or autosomal-dominant retinal vasculopathy with cerebral leukodystrophy, with structural protein dysfunction and perhaps with an embryonic syndrome that includes patent foramen ovale. Such a view makes the small excess stroke risk for young migraineurs unsurprising, and suggests a common genetics as opposed to a pathophysiological link for migraine pain. Remarkably, and importantly for patients and clinicians, the most recent

population-based epidemiological data suggest that migraine carries no excess risk for cognitive function compared with age- and sex-matched controls. In that French cohort, the presence or absent of changes in brain magnetic resonance imaging was also not predictive of cognitive decline ***(Tietjen et al., 2009).***

Familial hemiplegic migraine

In approximately 50% of the reported families, Familial hemiplegic migraine (FHM) has been assigned to chromosome 19p13. Few clinical differences have been found between chromosome 19-linked and -unlinked FHM families. Indeed, the clinical phenotype does not associate particularly with the known mutations. The most striking exception is cerebellar ataxia, which occurs in approximately 50% of the chromosome 19-linked, but in none of the unlinked families. Another less-striking difference includes the fact that patients from chromosome 19-linked families are more likely to have attacks that can be triggered by minor head trauma or are that associated with coma ***(Kors et al., 2009).***

Migraine aura

Migraine aura is defined as a focal neurological disturbance manifest as visual, sensory or motor symptoms. It is seen in about 30% of patients, and it is clearly neurally driven. The case for the aura being the human equivalent of the cortical spreading depression (CSD) of Leao has been well