INTRODUCTION

Cerebrospinal fluid (CSF) is a clear colourless body fluid produced in the choroid plexus of the brain. In humans, the rate of CSF production is 0.20-0.35 ml/min. It acts as a cushion or buffer for the cortex, providing a basic mechanical and immunological protection to the brain inside the skull and serves a vital function in autoregulation of cerebral blood flow. The CSF occupies the subarachnoid space and the ventricular system around and inside the brain and spinal cord ***(Ruggiero et al., 2010).***

Arachnoid granulations (Pacchionian granulations) are the major sites for the drainage of CSF into the blood. As CSF pressure increases, more fluid is absorbed. When CSF pressure falls below a threshold value, the absorption of CSF ceases. In this way, the CSF pressure is maintained at a constant level ***(Rosenberg et al., 2008).*** The total volume of CSF in an adult is 120 ml and the pressure is 150 mm of CSF with a range of 70-200 mm ***(Neville and Egan, 2010).***

CSF disorders occur as a consequence of disturbed normal CSF circulation, formation or absorption. CSF disorders occupy a very important position in the neurological practice, and can be classified as two major components, primary CSF disorders as Idiopathic intracranial hypertension (IIH), and secondry CSF disorders as postmeningitic hydrocephalus ***(Stephen et al., 2008).***

Headach is one of the most common clinical manifistation of altered Intracranial Pressure (ICP), the most

common types of CSF disorders are (IIH), with the incidence of 1.0 per100,000 in the general population, Normal pressure hydrocephalus (NPH) with the incidence of about 5.5 patients per 100,000 of people per year, Spontaneous cerebrospinal fluid leak syndrome (SCSFLS) that affects 5 out of every 100,000 people ***(Schievink, 2006).***

IIH sometimes called by the older names, benign intracranial hypertension (BIH) or pseudotumor cerebri (PTC), is a neurological disorder that is characterized by increased intracranial pressure in the absence of a tumor or other diseases ***(Binder et al., 2009)***. Papilledema is the hallmark sign of IIH, most patients (50%-94%) with papilledema have visual loss ***(Huna-Baron et al., 2006)***.

Although IIH may affect individuals of any age, most patients with this disease present in the third decade of life. Studies of American-based populations have estimated that the incidence of IIH ranges from 0.9 to 1.0 per 100,000 in the general population, increasing to 1.6-3.5 per 100,000 in women and to 7.9-20 per 100,000 in women who are overweight ***(Wall, 2008)***.

IIH has a strong predilection for women. More than 90% of patients with IIH are obese women of childbearing age ***(Fraser et al., 2010)***. However, men with IIH are twice as likely as women to lose visual function as a result of papilledema. Thus, the visual function of men with IIH must be followed more closely to avoid irreversible damage ***(Bruce et al., 2009)***.

If IIH presents in an individual who is not overweight, it is necessary to rule out associated risk factors, such as following exposure to or withdrawal from certain exogenous substances (eg, systemic steroids), obstruction of cerebral venous flow, and certain endocrine or metabolic disorders such as hypothyroidism ***(Monaghan, 2008)***.

Hydrocephalus refers to an excessive amount of cerebrospinal fluid within the brain's ventricles. Hydrocephalus has two major components which are: Communicating hydrocephalus, occurs when full communication occurs between the ventricles and subarachnoid space, and noncommunicating hydrocephalus, occurs when CSF flow is obstructed within the ventricular system or in its outlets to the arachnoid space ***(Rekate, 2009).***

Fetal hydrocephalus can represent as isolated ventriculomegaly, or secondry to other types of malformations, myelomeningocele, holoprosencephaly, Dandy-Walker syndrome, Joubert syndrome, arachnoid cyst, encephalocele, atresia of Monro and corpus callosum agenesis. Diagnoses can be made between 13 and 40 weeks of gestation (average 27 weeks) ***(Yamasaki et al., 2012).***

NPH is an important type of hydrocephalus that faces clinicians in daily practice. It affects older adults with a prevalence of 0.5% in those over 65 years old and an incidence of about 5.5 patients per 100,000 of people per year ***(Tanaka et al., 2009).*** There are 2 types of NPH: idiopathic and secondary. The secondary type of NPH can be due to a subarachnoid haemorrhage, head trauma, tumour, CNS infection, or a complication of cranial surgery ***(Rosenberg, 2008).***

NPH is a clinical symptom complex characterized by abnormal gait, urinary incontinence, and dementia. First described by Hakim in 1965, NPH describes hydrocephalus in the absence of papilledema. This concept was later modified to include patients with the above mentioned symptom complex, communicating hydrocephalus on imaging studies and normal CSF pressure on Lumbar puncture ***(Hakim and Adams, 1965).***

Spontaneous cerebrospinal fluid leak syndrome (SCSFLS) is a medical condition in which the CSF leaks out of the surrounding protective sac, for no apparent reason. SCSFLS afflicts 5 out of every 100,000 people. On average, the condition is developed at the age of 42, and women are twice as likely as men to develop the condition. Up to 94% of those suffering from SCSFLS are initially misdiagnosed. Incorrect diagnoses include migraines, meningitis, and psychiatric disorders ***(Schievink, 2006).***

SCSFLS is idiopathic; it can arise spontaneously or from an unknown cause. Various scientists and physicians have suggested that this condition may be the result of an underlying connective tissue disorder affecting the spinal dura ***(Louy and Schievink, 2007).*** Marfan syndrome, Ehlers-Danlos syndrome and autosomal dominant polycystic kidney disease are the three most common connective tissue disorders associated with SCSFLS ***(Liu et al., 2011).***Other studies have proposed that issues with the spinal venous drainage system may cause a CSF leak ***(Franzini et al., 2009).***

Brain Magnetic Resonance Imaging (MRI) with gadolinium is the diagnostic study of choice in the initial evaluation of patients suspected of having Spontaneous

intracranial hypotension (SIH). Characteristic MRI abnormalities such as diffuse gadolinium enhancement, subdural fluid collections or subdural hematomas, and sagging of the brain are secondary findings of SIH ***(Mokri, 2006).***

Radionuclide cisternography (RNC) and CT myelography are the spinal imaging studies used for identification of the actual site of a CSF leak. RNC performed by lumbar puncture injection of 110 MBq of 99mTc diethylenetriamine-penta-acetic acid (DTPA). Epidural blood patche (EBP) is the best choice in treatment of sever cases, performed with 10–20mL (mean 15 mL) of autologous blood at the site of CSF leak ***(Maya et al., 2008).***

Brain biochemical disturbances can be expected among patients with CSF disorders, including alterations of neuropeptide levels, as most CSF neuropeptides are derived from (CNS) sources ***(Lindefors et al., 2003)***. The implication of the presence of the octapeptide CCK-8 in a variety of brain functions, as well as its particular distribution in the human brain, has focused the interest of recent studies on investigating CCK-8 in NPH disorder. It shows significantly reduced mean value (0.79 -0.53fmol/mL) ($p = .002$) when compared to the control group (1.55 - 0.54 fmol/mL) ***(Galard et al., 2007).***

A recent study concerned with preoperative and postoperative 1H-MR spectroscopy changes in frontal deep white matter (FDWM) and the thalamus in NPH patients at 3 months postoperatively, shows no significant changes of N-acetyl aspartate (NAA) or total N-acetyl (tNA) in the thalamus. In contrast, in the FDWM, there was a significant increase of total choline (tCho) ($p=0.01$) and a borderline significant

decrease of myo-inositol(mIns) (p=0.06).Thus normalisation of thalamic tNA and NAA could not be detected postoperatively. The increased tCho and decreased mIns in the FDWM postoperatively might relate to clinical improvement ***(Lundin et al., 2012).***

Cerebral venography and manometry are used for the diagnosis of hemodynamically significant venous sinus stenosis in patients with the syndrome of IIH. Intravenous pressure measurements using the traditional microcatheter technique can be cumbersome, time consuming and potentially unreliable. Recently the Prime Wire Prestige pressure guidewire conducts pressure electrically and can be used as a guidewire for intervention ***(Lopes et al., 2012).***

Ventriculoperitoneal shunt is an ideal option of vast majority of patients with noncommunicating hydrocephalus. However, in case of availability of endoscopic facility and expertis‹ recently neuroendoscopic third ventriculostomy (ETV) has become a well-established procedure for the treatment of noncommunicating hydrocephalus as in cases of non-ruptured partially thrombosed giant basilar artery bifurcation aneurysm ***(Stachura et al., 2011).***

AIM OF THE WORK

Review of different types of cerebrospinal fluid disorders and updates in their management aiming for better diagnosis and treatment of these disorders.

FUNCTIONAL ANATOMY OF THE CEREBROSPINAL FLUID

CSF is a clear, colorless fluid that fills both the ventricles within the brain and the subarachnoid spaces around the brain and spinal cord. CSF is produced continuously, predominantly by choroid plexus within the lateral, third, and fourth ventricles. Choroid plexus consists of numerous villi, each composed of single-layer cubical epithelial cells around a core of highly vascularized connective tissue. An ultra-filtrate from the capillaries is processed by the epithelial cells and diffuses into the ventricles as CSF at a rate of 0.30 to 0.35 mL/min, or approximately 500mL/d, in children and adults. The total volume in children is 65 ml. The total volume of CSF in an adult is 120 ml and the pressure is 150 mm of CSF with a range of 70-200 mm ***(Neville and Egan, 2010).***

CSF normally is absorbed by arachnoid villi, diverticula of arachnoid that invaginate the superior sagittal sinus, and the major cortical veins along that sinus. Clusters of arachnoid villi, called arachnoid granulations, are visible to the naked eye. A layer of endothelial cells separates arachnoid villi from the systemic circulation. Equal production and absorption generate a CSF pressure of approximately 11cm H_2O ***(Cutler et al., 1968).***

CSF composition

It has been shown that the concentration of the different CSF components varies slightly depending on the site of CSF sampling. The exact measurement of the trace CSF composition would be achieved only through CSF sampling from the ventricles within the proximity of the choroid plexus ***(Welch, 1975).***

Table (1): A comparison between the concentration of electrolytes and protein in plasma and CSF ***(Greenberg, 2010).***

Constituent	Units	Plasma	CSF	CSF/Plasma Ratio
Osmolarity	mosm/liter	295	295	1.0
Water content		93%	99%	
Sodium	meq/liter	138	138	1.0
Potassium	meq/liter	4.5	2.8	0.6
Calcium	meq/liter	4.8	2.1	0.4
Magnesium	meq/liter	1.7	2.3	1.4
Phosphorus	mg/dl	4.0	1.6	0.4
Chloride	meq/liter	102	119	1.2
Bicarbonate	meq/liter	24	22	0.9
Pco2	mmHg	41	47	1.1
Ph		7.41	7.33	
Po2	mmHg	104	43	0.4
Glucose	mg/dl	90	60	0.67
Lactate	meq/liter	1.0	1.6	1.6
Pyruvate	meq/liter	0.11	0.08	0.73
Lactate/pyruvate ratio		17.6	26	
Total protein	mg/dl	7000	35	0.005
Total free amino acids	μmlo/dl	228	81	0.4
Ammonia	μg/dl	37	24	0.6
Urea	mmol/liter	5.4	4.7	0.9
Creatinine	mg/dl	1.8	1.2	0.67
Uric acid	mg/dl	5.50	0.25	0.05
Iron	μg/dl	15.0	1.5	0.01
Putrescine	pmol/ml		184	
Spermidine	pmol/ml		150	
Total lipids	mg/dl	750	1.5	0.002

It shows that although slight differences exist between electrolyte concentrations, the protein concentration of CSF is only 0.4% of the plasma. This means that there is no crystalloid osmotic gradient between plasma and CSF. On the contrary there is a moderate colloid osmotic gradient ***(Wood, 2006).***

The Ventricular System

The ventricles are the vestiges of the hollow tube that constitute the CNS in its embryonic stages. In higher vertebrates, they consist of four interconnecting cavities, the two lateral ventricles within the cerebral hemispheres, both of which open by the interventricular foramina of Monro into the single midline third ventricle which communicates through the aqueduct of Sylvius with the fourth ventricle ***(Davson, 1967).***

The lateral ventricles:

Each forms the cavity of a cerebral hemisphere and consists of:

The anterior horn is that part in front of the interventrricular foramen of Monro. It is bounded below by the rostrum of the corpus callosum, in front by the genu and above by the body, laterally is the head of the caudate nucleus, and medially the septum pellucidum.

The central part or body lies upon the thalamus and the caudate nucleus, below the corpus callosum, medial is the septum pellucidum and the fornix. The posterior portion of the central part divides at the so-called “trigone” into a posterior (occipital) and an inferior (temporal) horn ***(Rhoton, 2007).***

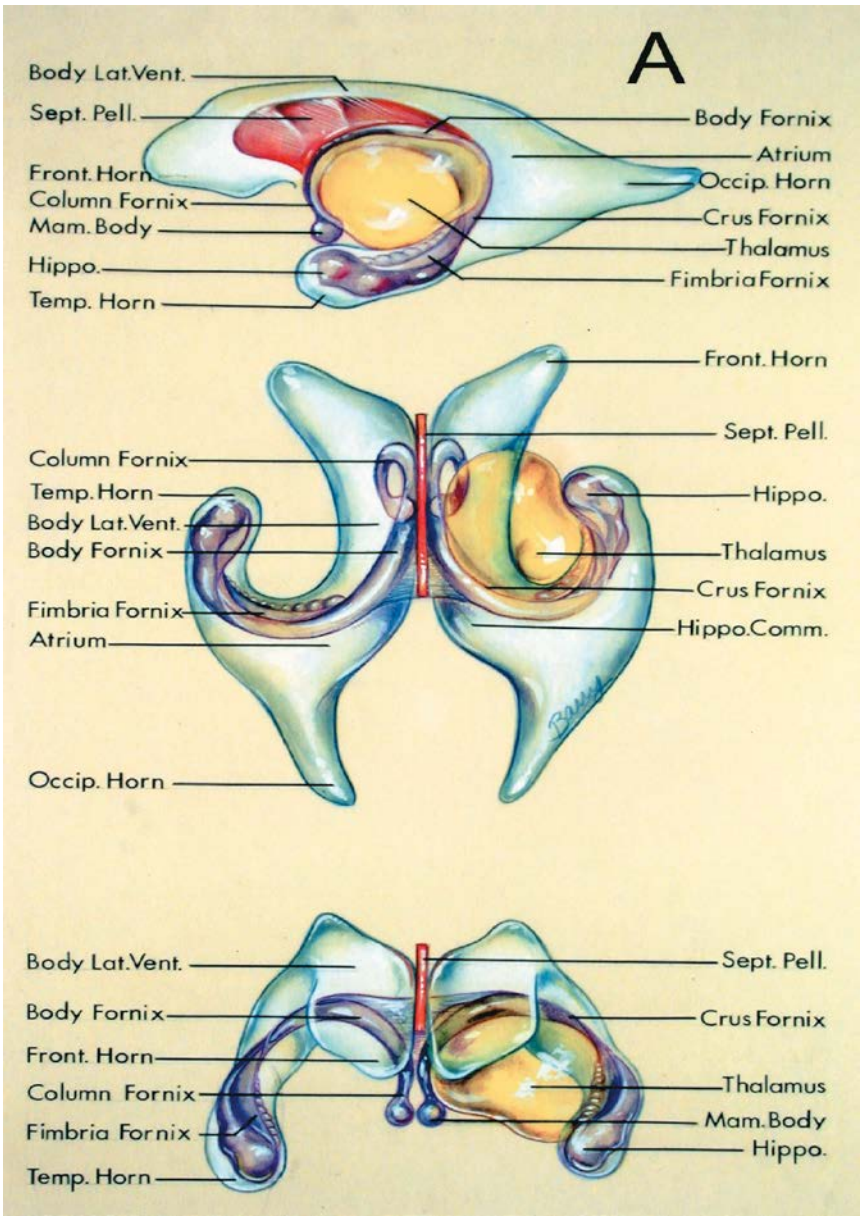

Figure (1): The Lateral ventricle ***(Rhoton, 2007).***

The posterior horns each of which passes backward into the occipital lobe being bounded above and laterally by the tapetum sheet of fibers of the forceps major (from the splenium of the corpus callosum) which forms an elevation, called the bulb of the posterior horn, in its wall.

Just below this elevation, a second one, the calcar avis, is associated with the calcarine sulcus on the medial surface of the occipital lobe.

The inferior horn extends downward, forward and laterally into the temporal lobe. Laterally are fibers of the tapetum, below is the hippocampus, and above is the tail of the caudate nucleus, which extends to the amygdaloidal body just in front of the tip of the temporal horn. The fibers of the optic radiation, arising from the lateral geniculate body, sways laterally above the temporal horn ***(Kier, 1977).***

The third ventricle:

It forms a narrow space that occupies the median plane in the diencephalon. Each lateral wall is formed by the thalamus above and the hypothalamus below, the division being marked by the hypothalamic sulcus ***(Voetmann, 1949).***

The two thalami are connected by the interthalamic adhesion or massaintermedia. The anterior wall is formed by the lamina terminalis, the floor by the hypothalamus, (a. optic chiasma, b. mamillary body, c. infundibulum, d. tuber cinereum) and the roof by ependyma and telachoroidea. The third ventricle presents the optic recess above the optic chiasma, the infundibular recess in the infundibulum of the hypophysis, the pineal recess in the stalk of the pineal body, and the suprapineal recess. Posteriorly, the third ventricle is continuous with the aqueduct of Sylvius that descends, through the posterior part of the midbrain to the fourth ventricle ***(Kier, 1977).***

The fourth ventricle:

The fourth ventricle is rhomboid in shape and is posterior to the pons and medulla oblongata. It is narrow below, where it is continuous with the central canal of the medulla. It is widest in its middle, where it is prolonged on each side as the lateral recess. Anteriorly the floor (rhomboid fossa); the pons above and the medulla below form it and is divided into right and left by the median sulcus. Posteriorly is the roof, which consists of sheets of white matter, (superior and inferior medullary vela), lined by ependyma, and concealed above by cerebellum. The lower part of the roof presents the median aperture (foramen of Magendie), and the far lateral end of each lateral recess present an opening, the lateral aperture (foramen of Luschka), by which the ventricular system communicates with the subarachnoid space ***(Foley and Baxter, 1958).***

Roof of the fourth ventricle

The roof of the fourth ventricle is tent shaped. It expands laterally and posteriorly, its narrow rostral end is just below the aqueduct, achieves its greatest height and width at the level of the fastigium and lateral recess, and then tapers to a narrow caudal apex at the level of the foramen of Magendie.

The inferior part of the roof is formed by thin membranous layers while the superior part is formed by thick neural structures. The external surfaces of the structures forming the superior part are intimately related to the cerebellomesencephalic fissure, and the structures forming the caudal part of the roof are intimately related to the cerebellomedullary fissure ***(Kier, 1977).***

The ventricular surface of the superior part of the roof is divided into a single median and two lateral parts. The median part is formed by the superior medullary velum, and the lateral parts, also called the lateral walls, are formed by the inner surface of the cerebellar peduncles. The superior medullary velum is a thin lamina of white matter that spans the interval between the superior cerebellar peduncles and has the lingula (the uppermost division of the vermis) on its outer surface. It is continuous at the fastigium with the inferior medullary velum.

The cisternal (external) surface of the structures forming the superior part of the roof also form the anterior wall of the cerebellomesencephalic fissure. This fissure is V-shaped when viewed from superiorly. The dorsal half of the midbrain sits in the limbs of the V-shaped notch, and the cerebellum forms its outer margin, with the apex being posterior. The inner wall of the fissure, which forms the outer surface of the superior part of the roof, is composed of the lingula, the dorsal surface of the superior cerebellar peduncles, and the rostral surface of the middle cerebellar peduncles ***(Matsushima and Rhoton, 2006).***

The neural structures separating the ventricular and cisternal surface of the superior part of the roof are thinnest in the area of the superior medullary velum and thickest in the area of the cerebellar peduncles. The rostral portion of each lateral wall, formed by only the superior cerebellar peduncle, is thinner than the caudal portion formed by the three cerebellar peduncles after they have united ***(Albert, 2012).***

The inferior part of the roof slopes sharply ventral and slightly caudal from the fastigium to its attachment to the inferolateral borders of the floor. The ventricular and cisternal

surfaces are formed by the same structures, the telachoroidea and the inferior medullary velum, except in the rostral midline, where the ventricular surface is formed by the nodule and the cisternal surface by the uvula. The choroid plexus is attached to the ventricular surface of the telachoroidea ***(Albert, 2012).***

The ventricular surface of the inferior half of the roof is divided into a cranial part, formed by the nodule and inferior medullary velum, and a caudal part formed by the telachoroidea. The inferior medullary velum is a membranous layer. It is a thin bilateral semitranslucent butterfly-shaped sheet of neural tissue that blends into the ventricular surface of the nodule medially and stretches laterally across the superior pole of the tonsil. The inferior medullary velum is continuous at the level of the fastigium with the superior medullary velum; caudally it is attached to the telachoroidea ***(Albert, 2012).***

The telachoroidea forms the lower part of the inferior half of the roof and the inferior wall of each lateral recess. It consists of two thin, semitransparent membranous layers, each about as thick as arachnoid, between which is sandwiched a vascular layer composed of the choroidal arteries and veins. The choroid plexus projects from the ventricular surface of the telachoroidea into fourth ventricle ***(Matsushima and Rhoton, 2006).***

The cisternal (external) surface of the lower half of the roof faces and is intimately related to the cerebellomedullary fissure. This fissure is one of the most complexes in the brain. Its ventral wall is formed by the posterior surface of the medulla, the inferior medullary velum, and the telachoroidea. Its dorsal wall is formed by the uvula in the midline and the