

## Hydrocephalus and Its Diagnosis - A Review

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### ABSTRACT

Hydrocephalus is enlargement of the ventricular system of the brain due to increased cerebrospinal fluid (CSF) volume and pressure. Congenital hydrocephalus is further classified as communicating and non-communicating depending on whether there is an obstruction to the flow of CSF or not.

Multiple causes have been identified in literature which has been summarized as an imbalance in the production and absorption of CSF. It can lead to cognitive impairment, cerebral palsy and visual field defects.

It is crucial to identify this condition prenatally as it can leave a debilitating impact on the fetus. Several modalities like ultrasound, computed tomography scans (CT) and magnetic resonance imaging (MRI) have been used to diagnose hydrocephalus. These can help reduce the disease burden and provide means for timely decisions.

**Key words:** Classification, Congenital Hydrocephalus, Diagnosis, Dilated Ventricles, Hydrocephalus, MRI, Prenatal, Ultrasound, Ventriculomegaly.

### INTRODUCTION:

Hydrocephalus is the enlargement of the brain ventricular system due to an excess in the volume of cerebrospinal fluid (CSF). This excess of CSF maybe due to an overproduction or poor reabsorption, which results in raised intracranial pressure (ICP)<sup>1</sup>. Accumulation of CSF in the subarachnoid space is called *external hydrocephalus*. Multiple causes have been identified in literature which have been summarized as an imbalance in the production and absorption of CSF.<sup>2,3,4</sup> Ventriculomegaly is a general term used for dilatation of ventricular system of the brain, irrespective of the cause.

Enlarged ventricles were identified by Hippocrates, Galen and Arabian physicians. It was then thought that this condition developed due to *extracerebral* collection of water.<sup>5</sup> However, Thomas Willis in the 17<sup>th</sup> century clarified the concepts of the ventricular system and in the 18<sup>th</sup> century important anatomical structures like the Aqueduct of Sylvius, foramen of Monroe and foramen of Magendie were identified by Francis Sylvius, Alexander Monroe and Francois Magendie respectively.<sup>2</sup> In 1886 Key and Retzeus documented the present-day concept of the flow of CSF. In 1913 Dandy and Blackfen were able to categorize and distinguish between communicating and non-communicating types of hydrocephalus.

The first sterile method for drainage of CSF by ventricular puncture was developed by Wernicke. Followed later by

serial punctures, eventually ventriculo-subarachnoid-subgaleal shunt was developed in 1893 by Mikulicz. These procedures were polished over the years and centuries and eventually the year 1950 led to the evolution of modern-day shunts.<sup>2,5</sup>

Cerebrospinal fluid is produced as an ultrafiltrate by the walls of the capillaries that are present in the choroid plexuses of the ventricles and is secreted by the action of  $\text{Na}^+/\text{K}^+$  ATPase pump present in the walls of these capillaries.<sup>4,6</sup>

Recent data suggests that CSF plays an essential role in homeostasis and neuronal functions. Therefore, any disturbance in its flow can result in hydrocephalus and also dementia if this condition occurs in adults.<sup>7,8</sup>

Walter Dandy developed experimental models to investigate the pathophysiology and treatment modalities for hydrocephalus in 1919. Based on these models the author was the first one to classify hydrocephalus as communicating and non-communicating.<sup>9,10</sup>

Various researchers have classified hydrocephalus is different ways, Raimondi explained it as “*water head*” and hence included all the conditions which were responsible for increased volumes of intracranial water under the heading of hydrocephalus. The author, therefore, not just included the actual etiologies responsible for causing hydrocephalus but also linked it to various conditions which were responsible for this vascular edema.<sup>11</sup>

Mori et al attempted to classify hydrocephalus based on the impact of treatment by studying 1450 patients in Japan.<sup>12</sup>

Oi and Di Rocco classified hydrocephalus in relation to the mechanism of obstruction to flow as primary, due to impedance to flow at a single point which included Arnold Chiari malformation and secondary hydrocephalus due to abnormal growth or hemorrhage.<sup>13</sup>

In a review article by Shakeri et al., hydrocephalus was classified based on the pressure of CSF as (i) normal pressure

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hydrocephalus, (ii) high-pressure hydrocephalus (iii) hydrocephalus due to aqueduct stenosis with a frequency of 47%, 27% and 15% respectively.<sup>4</sup>

Liu J and Rekate classified hydrocephalus into communicating, due to insufficient absorption of CSF in the subarachnoid space and obstructive or Non-communicating hydrocephalus due to a blockade in the flow of CSF from the ventricles to subarachnoid space. Obstructive type is further sub-categorized into a congenital and an acquired type.<sup>14,9</sup>

Kalyvas et al. describes congenital hydrocephalus as occurring in infancy and does not have any associated cause. However, when there is a known specific causative factor such as an invasive tumorous mass or an injury or insult to the brain, acquired hydrocephalus may occur.<sup>15,16</sup>

Tully in 2014 attempted to classify hydrocephalus in a simplified way which has been summarized in table 1.<sup>3</sup>

### Etiology:

Hydrocephalus presents a wide and comprehensive etiology which ranges from idiopathic, to structural defects to chromosomal anomalies. This wide array of etiology has been summarized in table 2.<sup>3,15,17,18,19,20,21,22,23</sup>

Maternal Risk factors are, diabetes, hypertension (pre-existing, gestational, pre-eclampsia and eclampsia), diabetes mellitus, gestational diabetes, pregnancy induced obesity, drugs (antidepressants, proton pump inhibitors (PPIs), nitrosatable drugs, metronidazole), maternal alcohol and illicit drug use and congenital infections<sup>19,24</sup>.

### METHODOLOGY:

Data Base Used: Google scholar, Pub- Med, Pak Medinet and ERIC.

Articles filter criteria: the used keywords generated about 100 articles ranging over a period of 20 years, the search was then tweaked and words like prenatal, dilated ventricle and ventriculomegaly were added. This resulted in reducing the number to about 70 articles. Out of these the articles ranging from 2010-2018 were selected. The abstracts and methodology of these articles were first read and eventually after going through the complete article they were finally selected. However, 2 articles from the years 1995 and 1999 were also included because of their relevance to the topic under review.

### DISCUSSION:

Incidence of congenital hydrocephalus was found to be maximum in Africa, followed by Latin America and lowest

Table 1: Classification of hydrocephalus

S. No.	Type of Hydrocephalus	Distinguishing Features
1	Acquired	Occurs as result of an extrinsic cause e.g. hemorrhage, infection, mass/ tumor etc.
	Congenital	Present at birth and is due to an intrinsic cause e.g. obstruction of aqueduct of sylvius
2	Obstructive / non-communicating	Obstruction of CSF pathway
	Communicating	No apparent source of obstruction identified
3	Syndromic	Hydrocephalus is present in association with other main physical characteristics
	Non-syndromic	Phenotype consists of findings only in the brain

Table 2: Etiology of Hydrocephalus

S. No	Type of Hydrocephalus	Etiology
1	Acquired	Hemorrhage, neoplasm, bacterial meningitis, cytomegalovirus, enterovirus, toxoplasmosis, prenatal intraventricular hemorrhage, drugs like misoprostol, metronidazole, antidepressants, isotretinoin
2	Obstructive / non-communicating	Aqueduct stenosis due to intrauterine hemorrhage or infections, obstructive intracranial cysts,
3	Communicating	Excessive CSF production, poor CSF reabsorption due to hemorrhage,
4	Syndromic	L1 cell adhesion molecule associated, Fried syndrome, Walker-Warburg/Muscle -Eye-Brain disease
5	Non-syndromic	Occurs with other brain lesions like holoprosencephaly, rhombencephalosynapsis, agenesis of corpus callosum, lissencephaly

Table 3: Classification of ventriculomegaly on prenatal ultrasound based on atrial measurements

Ventriculomegaly	Atrial diameter
Mild	10 -12 mm
Moderate	12.1-15 mm
Severe	>15mm

Table 4: Use of prenatal ultrasound in detection of hydrocephalus and other congenital anomalies

Title of study	Author	Journal & Year of publication	Method	Results
Correlation between prenatal diagnosis by ultrasound and fetal autopsy findings in second-trimester abortions <sup>21</sup>	Hauerberg et al	Acta obstetricia et gynecologica Scandinavica, 2012	52 pregnant females were included, ultrasound scans done between 11-13 weeks and 18-22 weeks. Results were correlated with autopsy findings	Full agreement b/w ultrasound & autopsy findings in 46% fetuses, in 90% main US findings were confirmed.
Comparison between prenatal ultrasound and postmortem findings in fetuses and infants with developmental anomalies <sup>31</sup>	Vogt et al	Ultrasound in Obstetrics & Gynecology. 2012	Retrospective review of 455 autopsies of fetuses and infants with congenital anomalies was conducted and compared with prenatal ultrasound performed by trained midwives and obstetricians	84% of prenatal ultrasound findings correlated with that of autopsy findings and statistically significant p values were obtained for 98% cases with main diagnosis.
Concordance between prenatal ultrasound and autopsy findings in a tertiary care center <sup>38</sup>	Rodrigues et al	Prenatal diagnosis. 2014	Retrospectively evaluated 151 elective termination of pregnancy and the findings were compared with ultrasound findings done between 11-13 weeks and 20-22 weeks	91.5% central nervous system, 91.3% renal system and 90.2% cardiovascular system anomalies were confirmed at autopsies, however, less correlation was found in musculoskeletal and abdominal anomalies.
Prenatal diagnosis of fetal ventriculomegaly: agreement between fetal brain ultrasonography and MR imaging. <sup>39</sup>	Perlman et al	American Journal of Neuroradiology. 2014	Prospective study in 162 fetuses, mean gestational age was 32 weeks, ultrasound was performed in axial plane and MRI was performed in coronal plane	Cut off for ventriculomegaly was kept at 10mm, the $\kappa$ -score was 0.94 for the narrow ventricle and 0.84 for wide ventricle. These results were in perfect harmony thereby establishing the concordance between the two modalities
Accuracy of prenatal diagnosis of isolated aqueductal stenosis. <sup>36</sup>	Emery et al	Prenatal diagnosis. 2015	Retrospective study, stenosis of aqueduct of Sylvius was detected prenatally in fetuses with ventriculomegaly by ultrasound and MRI and compared with findings on postnatal MRI and CT scans	All 6 cases of isolated Aqueductal stenosis and 6 cases of aqueductal stenosis with associated anomalies were accurately identified and confirmed by postnatal MRI and CT scans
Neurological outcome in fetuses with mild and moderate ventriculomegaly <sup>40</sup>	Tonni et al	Revista Brasileira de Ginecologia e Obstetricia. 2016	62 fetuses diagnosed as mild and moderate hydrocephalus on prenatal ultrasound and results were compared with fetal and postnatal MRI	Bilateral ventriculomegaly was identified in 58% of fetuses and this finding was later supplemented and supported by MRI findings in 85% of cases.

in USA, 316, 145 and 68 per 100,000 births. A prevalence of 0.34/1000 births was noted in Nigeria.<sup>25</sup> Male predilection was also observed by Dewan et al in their metanalysis study.<sup>26,27</sup> Another author observed a relationship between male gender and the development of intracranial hemorrhage which is a risk factor for developing fetal hydrocephalus.<sup>19</sup>

Age specific metanalysis study conducted by Isaac et al reported highest prevalence of 88/100,000 in pediatric age group followed by 11/100,000 in adults; and 175/ 100,000

in the elderly.<sup>28</sup> Munch et al in their study found a prevalence of 1.1/1000 live births out of which 75% had a positive family history.<sup>29</sup> A very high prevalence of 4 -12/ 10000 live births was observed in China as compared to European countries. The authors also observed a decline in congenital hydrocephalus because of widespread use of folic acid as part of antenatal care.<sup>30</sup> Both studies found a higher prevalence of hydrocephalus in low income countries as compared to high income countries.<sup>31,32</sup>

Liu J, in 2018 reported the prevalence rates of 4.65 per 10,000 (European regions), 11 per 10,000 (Denmark) 5.9 per 10,000 births (California) and 7 per 10,000 births (China).<sup>14</sup> An incidence of 1 in 10,000 live birth is reported in Pakistan by Salat et al.<sup>33</sup>

Ninety nine percent women undergo prenatal ultrasound scans as part of normal routine during pregnancy. With advances in technology, the enhancement of experience and skills of sonologists the accuracy with which ultrasound scan can detect prenatal anomalies has increased over the decade.<sup>31,32</sup> Ultrasound scans have proven to be a safe, useful, easiest and most sensitive test for the diagnosis of hydrocephalus.<sup>34</sup> Addario et al., identified the sensitivity of ultrasound to diagnose ventricular enlargement as 93.5 %, especially if scans are done at 24 weeks of gestation or later. Sensitivity of the scans drop to 35% if done before 24 weeks of gestation. This difference in sensitivity, as stated by Addario et al., is most likely due to the course of disease itself rather than any errors of measurement.<sup>35</sup>

The size of lateral ventricle should be measured as part of routine screening done in second trimester. Scans done in axial plane maximize the visualizations of frontal horns, septum pellucidum and the atria of the lateral ventricles.<sup>34</sup> The part of lateral ventricle where the body, posterior horn and inferior horn meet is called the atrium of the lateral ventricle.<sup>17</sup> Between 15 – 40 weeks of gestation the atrial width remains constant, that is < 10mm. Any increase in this measurement leads to ventriculomegaly which is classified by atrial width measured on ultrasound.<sup>17,34,36,37</sup> Details of these measurements are described in table 3

Several researchers have compared the results of prenatal ultrasound with MRI and postnatal autopsy results which have been summarized in table 4.

Hydrocephalus has been known to be associated with several other congenital anomalies which can be easily detected on prenatal ultrasound. Study conducted by Mahmoud et al in Sudan found stenosis of aqueduct of Sylvius to be most commonly and frequently associated anomalies (45%) followed by spina bifida (30%), Arnold Chiari malformation (20%) and Dandy Walker formation (5%).<sup>41</sup> Ventricular septal defect, tetralogy of Fallot, diaphragmatic hernia, gastroschisis, hydronephrosis, urinary malformation are a few others which have been found to be associated with hydrocephalus.<sup>31,32</sup>

Literature has identified shunt systems and endoscopic 3<sup>rd</sup> ventriculostomy as treatment modalities for hydrocephalus.<sup>2</sup> Recurrence risk of hydrocephalus was found to be 55.6% in same sex twin, 6.6% in first degree relative, 2.1 % in second degree relatives and 1.7% in third degree relatives.<sup>28,42</sup>

Impact of untreated hydrocephalus depends on the severity of the hydrocephalus. It can lead to cognitive impairment, cerebral palsy and visual field defects.<sup>28,42,43</sup> Abnormal neurodevelopment is associated with mild to moderate

hydrocephalus in 7 -8 % fetuses whereas with severe hydrocephalus in 58% fetuses.<sup>36</sup>

## CONCLUSION:

Ventriculomegaly or hydrocephalus can easily be identified in second trimester by transabdominal scans since it can lead to a multitude of neurodevelopmental disorders. Therefore, its early detection and screening is advised. CT scans can diagnose hydrocephalus and other anomalies as efficiently as ultrasound however it has risk of exposing the fetus and mother to radiations. Above all, this modality has high cost and lack of availability concerns attached to it in a developing nation such as ours. MRI is another significant tool to diagnose hydrocephalus, a coherence was identified in both modalities' ultrasound and MRI, thereby enhancing the counselling and the pre and post-natal management of the patients.

Ultrasound remains as one of the cheapest, cost effective, easily accessible and most sensitive modalities which can prove to be of great value in detecting hydrocephalus. This in turn can allow the physicians and parents to make timely decisions regarding rehabilitation or termination of pregnancy thereby reducing the disease burden in the society.

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