HYDROCEPHALIC CHILDREN PRESENTING TO A MALAYSIAN COMMUNITY BASED UNIVERSITY HOSPITAL OVER A 9 YEAR PERIOD.

Khairi Salleh MD\textsuperscript{x}, J. Abdullah\textsuperscript{0} MD, Phd. Diplomate Neurosurgery (Belgium) AM (Mal), FICS (USA).

\textsuperscript{x}Klinik Saleha, Bachok, Kelantan, Malaysia.
\textsuperscript{0}Neurosurgical Unit, Department of Surgery, Hospital University Science Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia.
Abstract

There are few local statistics on the incidence of hydrocephalus and the outcome of hydrocephalic shunts done in the South East Asian region. We report a retrospective study of 285 hydrocephalic patients who underwent shunting procedures between 1990 and 1998 at the Hospital University Sains Malaysia. This study ascertains the incidence of shunt infection and developmental outcome of these patients in relation to various factors. All records were traced via our computerized registry. Followup questionnaires were sent to all patients enquiring about their abilities to perform daily activities and assessed using the Denver Developmental Screening Test.

The incidence of shunt infection was higher in the younger age group (60\% between the age 3 and 4 months). Poor preoperative skin condition, type of operation (primary insertion versus revision versus insertion after infection) and the presence of postoperative wound dehiscence or scalp necrosis were important associated factors. In hydrocephalus which was diagnosed antenatally, 50\% had normal performance and the development was considered normal. Majority of patients undergoing surgery within first week of admission had a good outcome. The presence of other congenital abnormalities was strongly correlated with poor developmental outcome.

Antenatal ultrasound is important to identify high risk groups and suggest hospital delivery in a hospital with neurosurgical facilities or early referral to neurosurgical unit which would improve outcome in these cases. Developmental outcome is better in hydrocephalus not associated with other anomalies and has no relationship to the cortical thickness.

Key words: hydrocephalus, etiology, incidence, developmental outcome, shunt, Kelantan.
Introduction

Hydrocephalus is defined as a bicaudate index above the 95th percentile of age\textsuperscript{1}. It is marked by the excessive accumulation of cerebrospinal fluid within the ventricles. The disorder is characterized by an imbalance in the production and/or reabsorption of cerebrospinal fluid. Whereas this excess in fluid usually leads to an elevation of intracranial pressure, compensatory adjustments occur, especially in very young and very old subjects, that can reduce prevailing cerebrospinal fluid pressure to a normal range.

Congenital hydrocephalus is usually the result of an intrauterine infection or maldevelopment of the aqueduct of Sylvius. Acquired hydrocephalus can be caused by infection, neoplasm or hemorrhage\textsuperscript{2-3}. In infants, hydrocephalus usually presents as progressive head enlargement\textsuperscript{4}.

The presenting symptoms in children are irritability, headache, nausea, vomiting and lethargy. Diagnosis is made with ultrasonography, computed tomography or magnetic resonance imaging. The majority of patients are treated with cerebrospinal fluid shunt procedures, most commonly the placement of ventriculoperitoneal or lumboperitoneal shunts.

The outcome of hydrocephalus is determined by the etiology, the presence or absence of associated anomalies of the brain, and the timeliness of diagnosis and treatment. This paper aims to study the epidemiology of hydrocephalus and complications associated with shunt procedures. It also aims to establish the factors associated with shunt infection and to study the prognostic factors which determine the patient’s developmental outcome.

Material and Methods

This was a retrospective study over 9 years. Details of all patients listed under ICD-9:742.3 (Hydrocephalus) were obtained from the record office. Only those patients who had ventriculoperitoneal shunt were included in this study. Children up to the age of 13 years were included as defined by the Malaysian legal system.

In order to study the prognostic factors which determine the patient’s developmental outcome, followup questionnaires were sent to all patients who were discharged alive enquiring about their ability to perform daily activities. All the patients
were seen at neurosurgical outpatient clinic and were tested using Denver Developmental Screening Test.

The developmental score was based on the performance of the children: the score for normal performance, doubtful performance and abnormal performance was 1, 2 and 3 respectively. The scoring was carried out in four categories: gross motor, fine motor, audiovisual (language) and psychosocial performance according to the age of the patient.

Score 1 was given if a child performed the tested items and the development was considered normal. Score 2 was given when a child passed a part of the tested items and score 3 was given when a child failed the tested items and the development was considered abnormal. Using the prepared study protocol, relevant data were collected and later analysed.

Results

During the period studied from January 1990 to December 1998, there were 285 patients (new cases) admitted to the Hospital Universiti Sains Malaysia with a diagnosis of hydrocephalus. There was a male preponderance (1.7:1) in this study. Of the 285 patients, 215 (75.5%) were males and 70 (24.5%) were females. Two hundred and fifty seven (90%) patients were Malays, 15(5.3%) Chinese and 1(4.7%) Indian. Eighty-six (30%) patients were between 0 and 30 days of age. One hundred (35%) patients were between 31 days and 365 days, 80 (28%) were between 1 year and 5 years and 19 (6.7%) patients between 5 years and 13 years. One hundred and fourteen (40%) patients were from Terengganu and the remainder from Kelantan. In 174 (61%) cases, hydrocephalus was due to congenital abnormalities of which aqueductal stenosis was the commonest (3.4%) followed by Dandy Walker variants (28.7%) and others (e.g. Schizencephaly, holoprosencephaly) which accounted for 64 cases (36.8%). Neoplasm was found in 10 cases (3.5%) and post-meningitic hydrocephalus was found in 50 cases (17.5%). In 5 (1.8%) patients hydrocephalus was caused by trauma and 46 patients had non-traumatic intraventricular hemorrhage. Thirty-five cases (12.3%) of hydrocephalus were diagnosed antenatally. One hundred and sixty cases (56.1%) were diagnosed before 30 days of age 90 cases (31.6%) were diagnosed after age of 1 month.
Fourteen (4.9%) hydrocephalus patients in this study were associated with lumbosacral myelomeningocele and encephaloceles. Eighty-four (29.4%) hydrocephalus patients were born premature and 201 (70.6%) were born full term.

The timing of surgery in this study was calculated in days from the time of admission till the time of operation. In 153 cases (53.7%) the operation of ventriculoperitoneal shunt was done early within the first week of admission (D1-D7). In 49 (17.2%) cases, ventriculoperitoneal shunt was done within second week of admission (D8-D14). In 28 (9.8%) cases ventriculoperitoneal shunt was done within third week of admission (D15-D21). Fifty (7.5%) cases of ventriculoperitoneal shunt were done within fourth week (D22-D28) of admission. These were cases of congenital hydrocephalus associated with infected preoperative encephaloceles, chronic meningitis, and lumbosacral myelomeningoceles where VP shunt was delayed. In all 285 cases computed tomographic scan of the brain was done. The cortical thickness (in mm) was measured from all the computed tomographic scan films. This measurement was done at the parietal area following the scale in the film. Of 285 cases, 101 cases had cortical thickness measurement of < 10 mm. Cranial ultrasound was done in 167 (58.5%) patients, of which intra uterine ultrasound were done in 35 (12.3%) patients.

Seventy-seven patients (27%) had birth weight less than 2.0 kilogram and 150 (52.6%) babies weight between 3.0-3.4 kilograms. The presenting features were increase head size (93.3%), fever (19.6%), fits (16.9%), vomiting (7%) and drowsiness (12.2%).

At presentation, 186 (65.3%) patients were found to have separated sutures in which the head circumferences were above the 90th centile. All of them were younger than one year of age.

All these patients underwent ventriculo-peritoneal shunt as a primary procedure. 35 (12.2%) patients underwent revision of the shunt due to shunt blockage and 10 (3.5%) patients underwent reinsertion of ventriculoperitoneal shunt after shunt infection settled.

In ten cases, repair of myelomeningocele and encephaloceles was done earlier before ventriculoperitoneal shunt due to cerebrospinal fluid leakage. Ventriculoperitoneal shunt was done in these patients 2 weeks later when hydrocephalus was noted. In four cases, repair of myelomeningocele was done together with ventriculoperitoneal shunt. No shunt infection was related to myelomeningocele or encephalocele repair procedure. Two
hundred and twenty eight (80%) received medium pressure paediatric shunts: 29 (10.1%) received low pressure and 28 (9.9%) received high pressure shunts. Shunts were the unitized type for all shunt pressure from Radionics®, Medtronic® or Baxter®. Only 29 cases (10%) received the Delta shunt® from Medtronic. There were no significant different in all three shunts systems and operative complications.

Shunt infection from primary shunt insertion was recorded in 10 (3.5%) patients. Most of them presented with pus discharge from the scalp wound or from the abdominal wound. Pathogens isolated were S. Aureus in 9 (3.2%) cases and Pseudomonas aeruginosa in 1 (0.3%) case. Blocked ventriculoperitoneal shunts were recorded in 35 (12.2%) patients over a mean followup period of 5 years.

Meningitis was recorded clinically in 36 (12.6%) patients. Five patients (1.8%) were recorded to have peritonitis or septicaemia associated with shunt infections. Most of the shunt infections were seen in children less than 6 months old. Out of 10 (3.5%) cases, 3 (1%) were patients age less than 1 months and 7 (2.5%) were patients age 2 to 3 months.

All ten cases of shunt infection were associated with wound dehiscence or scalp necrosis post operatively. In 5 cases (1.8%) there were extraperitoneal migration problems of the peritoneal catheter in the scrotum (two cases), rectum (one case), extravaginal (one case) and right supradiaphyramatic pleural cavity effusion.

A follow-up period of more than 6 months was obtained for 65 patients, 4 years for 114 patients and 8 years for 106 patients. Eighteen (6.3%) of the patients died during follow-up. All cases of death were attributed to sudden death. No autopsies were done in these eighteen cases. These cases had abnormalities around the brain stem such as Dandy Walker Syndrome or its variant.

Post operative craniosynostosis were seen in 29 cases (10%) of which 12 (4.2%) were plagiocephaly, 10 (3.5%) were turricephaly and 7 had other forms of cranial abnormalities. This pathology was noted at a mean interval of 4 months after ventriculoperitoneal shunt. Twenty-six cases (90%) were due to unitized medium pressure shunts from various manufacturers and 3 (10%) were from low pressure shunts.

Table 1 and 2 describe the relations of performance to time of diagnosis and time of surgery.
Figure 1 shows the correlation between the hydrocephalus associated with congenital anomalies. Out of 174 cases, 69 (39.7%) patients have doubtful performance, 52 (29.9%) patients have abnormal performance and normal developmental outcome were recorded in 53 patients (30.5%).

Table 3 shows the association of hydrocephalus with cortical thickness and congenital anomalies.

Discussion

Attitude of parents towards modern medicine is a major factor contributing to the outcome of treatment as compared to that of many other centres. Their strong belief in traditional (faith) healers results in late presentation and refusal towards treatment offered. It is not uncommon to find a patient with huge hydrocephalus due to parents refusal for surgery. Epidemiological trends and etiologies have previously been investigated in population-based studies on infantile hydrocephalus in other centres.5-9

The overall incidence of hydrocephalus in the general Malaysian population is not known. Since the condition occurs in association with a large number of childhood and adult intracranial diseases, it is obvious that the reported incidence of infantile hydrocephalus, namely 3 to 4 per 1000 live births, is grossly understated.2 The overall prevalence per 1000 livebirths was 0.53, with a slightly increasing trend from 0.48 to 0.63. The increase was entirely referable to the preterm group and there was no tendency to an increase in the term group.2,5-10

Common etiologies of hydrocephalus11-20 are shown in Table 4.

The results from the retrospective analysis of shunt procedures over the past few years confirmed an age dependent effect on the operative shunt infection rate. Children in the 1 to 6 month age range have a significantly higher chance of developing infection/colonization of their shunt than those older than 6 months. This period of increased susceptibility to shunt infections has previously been thought to be due to a relative deficiency of the immune response against bacteria.21-22

The level of maternal immunoglobulin G (IgG) decreases rapidly during the first year of life and there is a period (2 to 6 months) when infant IgG levels are less than 50% of normal adult levels. Complement activity in neonates is much lower than that in adults
and the white cell capacity for dealing with infecting organisms is less efficient. Renier et al,\textsuperscript{23-24} believed that those factors and the period of lowered IgG in children between 2 and 6 months of age were responsible for the high incidence of shunt infection.

An alternative explanation for the increased CSF shunt infection rate in young infants comes from the age-related changes in the skin and its resident bacterial flora. Leyden and colleagues\textsuperscript{25} carried out a quantitative study of the levels of resident aerobic and anaerobic bacteria on the faces of volunteers of different age. They found the density of aerobic cocci and Propionibacterium acnes was higher in infancy than in early childhood. In their study, they also found a higher bacterial density on the head than on the trunk or limbs.

Similar results were obtained by Selwyn and Ellis\textsuperscript{26} in their study of skin bacteria and wound contamination. The bacterial colonization of neonate occurs very rapidly after birth as a result of passage through the birth canal and subsequent exposure to the local environment. Skin Staphylococci are present at birth in small numbers, but their density increases steeply during the first 48 hours to reach a plateau at the end of this period.

Significantly different infection rate were also observed depending on the end of the shunt revised.\textsuperscript{27} Infection was three times more frequent after manipulation of the ventricular catheter than after revision of only the distal end (atrial or peritoneal catheter). However this factor was not studied due to lack of post-operative recording of ventricular or peritoneal catheter during shunt revision.

In our series, there is no correlation between the cause of hydrocephalus and the infection rate although the infection rate was higher in post meningitis hydrocephalus. Our overall rate of 4\% is lower compared to the others.\textsuperscript{28-30} All the pathogens were detected in lumbar puncture fluid, shunt reservoir puncture fluid or pus swab for culture and sensitivity. No growth was found in most cases of shunt tip for culture and sensitivity and also from pus swab for culture and sensitivity, which could explain the overall lower rate of detection.

Staphylococci was involved in the majority of shunt infections in this series. In the literature, Staphylococcus epidermidis accounts for the very large majority of ventriculo-atrial shunt septicaemia. No VA shunts were done in this study, so the distribution of pathogens cannot be studied in this group. Staphylococcus epidermidis
was the most common bacterium in patients with meningitis, while Staphylococcus aureus was isolated mainly in cases of wound sepsis.

Post operative wound dehiscence or a scalp necrosis significantly increased the infection rate in this study. All patients with scalp necrosis or wound dehiscence became infected compared to 16.7% of patient who did not have any skin problems postoperatively.

Obstruction of the shunt in hydrocephalic patients, which causes the hydrocephalus to recur, can present different manifestations. In the slit ventricle syndrome, the ventricles fail to dilate and remain small or slit-like despite increased intracranial pressure. Shunt obstruction can also induce CSF edema along a catheter inserted into the ventricles rather than in the periventricular space.\textsuperscript{31-35}

It has been suggested that all children under the age of 6 months undergoing shunt surgery should be targeted for antibiotic prophylaxis in view of their much higher infection rate. However, the evidence to support the routine use of antibiotics in shunt surgery is weak.\textsuperscript{29-30,38} Despite the number of investigators who have compared the prevalence of infection in patients with and without antibiotic coverage, no study withstands scientific scrutiny and most of the early trials were reported as sequential studies.\textsuperscript{39-41,56-57}

There is strong experimental and clinical evidence that the treatment of grossly contaminated surgical wounds with topical antibiotics by the application of antibiotic powder or solution effectively reduces the expected wound infection rate. There is some evidence to suggest that clean contaminated wounds with an expected risk of infection greater than 5% to 15% may benefit from the topical application of antibiotics. There is no sound clinical or experimental evidence demonstrating the effectiveness of topical antibiotics in preventing wound infection in clean or clean-contaminated wounds with an expected infection rate of less than 5%.\textsuperscript{53}

The most widely used instrument for developmental screening is the Denver Developmental Screening Test (DDST).\textsuperscript{58} The DDST was not developed to predict developmental outcome, but the literature and clinical experience suggest that referrals for intervention or special education are often based solely on DDST results.\textsuperscript{59-62}
Generally, Malaysian and Denver children appear to be similar on their development during the first six years of line except for some minor differences in the personal social, language and gross motor sectors. The differences in development between the two groups of children can partly be explained by differences in socio-economic or cultural differences.63

The American Academy of Pediatrics has recommended a two-step screening process by which development in all children is checked through parent report and examination of the child. The purpose of the initial screening is to identify most children with delayed development: thus it must be quick, simple, and accurate.

Use of the key DDST items is an economical and efficient way to screen the development of young children. Experience suggest that 25 hours would be saved in screening 100 children with these items instead of the full DDST. To facilitate the use of the key DDST items, DDST forms are now being printed with bold outlines around the 39 key items. Shortened forms have been developed and validated for concurrent cognitive deficits.58

The predictive validity of the Denver Developmental Screening Test (DDST) were evaluated by Greer S et al.59 They concluded that for children over three years of age: the DDST is specific (94 percent of the children with a good outcome were categorized as normal); the DDST is not sensitive (it did not identify 80 per cent of the children who later had a poor outcome); a child with a poor outcome was 14 times more likely to have an abnormal or questionable DDST result than a normal one.

These suggest that a child with an abnormal DDST is likely to have a poor school outcome and that many children with school-related problems who might benefit from early intervention are not identified by the DDST.

The majority of infants presenting with progressive hydrocephalus are now treated surgically with ventricular shunting. It is difficult to predict the eventual developmental outcome of most treated patients. The outcome of hydrocephalus was reviewed in infancy and childhood. It was determined by the etiology, the presence or absence of associated anomalies, and the timeliness of diagnosis and treatment.59-61

The neurological outcome has been reported to be very poor in X-linked hydrocephalus.14 Even though shunts were placed in early infancy, shunt procedures did
not improve the patients neurological condition except for preventing progressive macrocephaly. Thus, diagnostic methods for fetal hydrocephalus, especially X-linked hydrocephalus, early in pregnancy would be very useful.

The infants presenting with hydrocephalus at birth were also reviewed in order to evaluate the functional results. The importance of head enlargement at birth, ventricular size, and the age at the time of surgery are not related to late functional results. The results were best when there were no associated malformations, no shunt infection, when hydrocephalus was due to aqueductal stenosis, or when the first developmental quotient measured at 6 months was over 80.

The long term outcome of infantile hydrocephalus in children born at term during a period of active shunt treatment was studied in a population-based survey by E. Fernell et al. They concluded that the single most important factor for the outcome of infantile hydrocephalus was found to be the presence or absence of associated primary brain damage or maldevelopment.

Compared with infantile hydrocephalus children born at term, preterm children with infantile hydrocephalus had a considerably poorer outcome. The mortality before the age of two among preterm children surviving two years of age, 60% had at least one additional neuroimpairment, whereas the corresponding figure for term infantile hydrocephalus children was 45%. The proportions of CP, mental retardation and epilepsy among preterm infantile hydrocephalus were 47%, 51% and 33%, compared with 28%, 38% and 22%, respectively, in the term infantile hydrocephalus group.

The differences in the neurodevelopmental outcome between term and preterm infantile hydrocephalus children might be explained by the stage of brain maturation and vulnerability at the time of the specific negative event, and by the type, location and extent of the lesions. The difference between preterm infants and those born at term regarding the site of cerebral vascular insults. In the preterm infant the target area susceptible to hypoxic or hemorrhagic perinatal brain lesions is the periventricular white matter, and in term infants the cortex and basal ganglia.

Meanwhile, the neurodevelopmental outcome of periventricular hemorrhage and hydrocephalus in a regional population of very low birth weight infants was studied by
William C. Hanigan et al.\textsuperscript{15} They found that the risk of abnormal neurodevelopmental outcome was elevated for all grades of periventricular hemorrhage. A 12\% incidence of hydrocephalus was associated with high-grade periventricular hemorrhage and appropriate treatment did not alter the poor prognosis. Intra uterine treatment of fetal cerebral ventriculomegaly has been largely abandoned, as the results have been disappointing compared with those of standard neonatal treatment. The natural history of ventriculomegaly diagnosed in utero has not been studied adequately and that fetal surgery may have a role in selected patients. Drugan A et al.\textsuperscript{64} analyzed the outcome of fetal ventriculomegaly followed up without active treatment in utero. They suggest that the prognosis is poor for fetuses with ventriculomegaly and coexistent malformations, good for those with isolated, non progressive ventriculomegaly, and variable for those with progressive, isolated ventriculomegaly.

\textbf{Conclusions}

The study has shown an association between infection rate and two factors: type of operation (whether primary insertion, revision, or reinsertion after infection); and the presence of postoperative wound dehiscence or scalp necrosis. Early surgical intervention is needed if there is no other contraindication. Refusal by parents for surgical intervention seen in 30\% of cases may lead to abnormal performance. Basic health education is one way to improve the knowledge of public in regards to the correct management of hydrocephalus. The cortical thickness has no significant relevance with the developmental outcome.

The results are good in congenital hydrocephalus without anomalies and indirectly proportionate to the number of revision. It is important to identify the high risk group by regular antenatal ultrasound and suggest hospital delivery for the risk group or those antenatally diagnosed with hydrocephalus.
Reference.


Table 1
Performance related to age at detection and timing of surgery.

<table>
<thead>
<tr>
<th>Age of detection</th>
<th>Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td>Antenatal (n=35)</td>
<td>18 (51.4%)</td>
</tr>
<tr>
<td>0-30 days (n=167)</td>
<td>49 (29.3%)</td>
</tr>
<tr>
<td>&gt; 30 days (n=83)</td>
<td>25 (30.1%)</td>
</tr>
</tbody>
</table>

Table 2.
Performance related to timing of surgery

<table>
<thead>
<tr>
<th>Timing of surgery</th>
<th>Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td>(i) Operation within one week of admission (n=153)</td>
<td>61 (39.8%)</td>
</tr>
<tr>
<td>(ii) Operation within two weeks (n=49)</td>
<td>25 (51%)</td>
</tr>
<tr>
<td>(iii) Operation after 2 weeks (n=33)</td>
<td>-</td>
</tr>
<tr>
<td>(iv) Operation done after 4 weeks of admission (n=50)</td>
<td>-</td>
</tr>
</tbody>
</table>
Table 3.
Hydrocephalus versus cortical thickness and association with congenital anomalies.

<table>
<thead>
<tr>
<th>Cortical thickness and congenital abnormality</th>
<th>Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td>Cortical thickness less than 10 mm (n=101)</td>
<td>34 (33.7%)</td>
</tr>
<tr>
<td>Cortical thickness more than 10 mm (n=184)</td>
<td>37 (20%)</td>
</tr>
<tr>
<td>Congenital malformation</td>
<td></td>
</tr>
<tr>
<td>Present (n=174)</td>
<td>53 (30.5%)</td>
</tr>
<tr>
<td>Absent (n=111)</td>
<td>100 (90.1%)</td>
</tr>
</tbody>
</table>

Table 4.
Causes of hydrocephalus

(i) Non-acquired
   a. X-linked
   b. Specific central Nervous system anomalies

(ii) Acquired
    a. Intracranial bleeding
    b. Trauma
    c. Meningitis
    d. Tumours