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The effect of cerebrospinal fluid's biochemical and cellular properties on ventriculoperitoneal shunt survival

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Abstract

Background: The burden of hydrocephalus in our region is huge. Ventriculoperitoneal (VP) shunting is the main mode of treatment of hydrocephalus. These shunts frequently malfunction, with shunt blockage being the commonest cause of shunt failure. The biochemical and cellular properties of CSF are hypothesized to contribute to shunt blockage. This study aimed to demonstrate the impact of these CSF properties on shunt survival. **Materials and methods**: This was a prospective cohort study. Patients were recruited into the study following VP shunt surgery for hydrocephalus. Based on their baseline CSF biochemical and cellular properties, the patients were divided into two groups; those with normal and those with abnormal CSF biochemistry and cellularity. Patients were then followed up in the neurosurgical clinics for a period of 3months during which shunt function was assessed clinically. This data was then entered to the statistical package for social sciences (IBM SPSS statistics 25.0) for data analysis. **Results**: A total of 82 patients met the inclusion criteria and were recruited into the study. Forty-six (56.1%) were male while 36(43.9%) of them were female. The mean age was 15.5 months (SD 23.4 months). Majority (82.9%) of the patients had congenital hydrocephalus with Dandy walker malformation being the most common congenital anomaly seen. Most patients (52.44%) had normal CSF proteins while the remainder had elevated CSF proteins. Majority of the patients had reduced levels of CSF glucose at 65.9%. The CSF cell count was normal for most of the patients at 86.6%. Elevated CSF protein concentration was associated with an increased likelihood of ventriculoperitoneal shunt failure by 8.7 times compared to the patients with normal CSF protein concentration. Reduced CSF glucose concentration was associated was also found to increase the likelihood of shunt failure in this study. There was no correlation between the CSF cell count and the likelihood of shunt failure.

Key words: *Hydrocephalus, CSF biochemistry and cellularity, ventriculoperitoneal shunt survival*

Introduction

Ventriculoperitoneal (VP) shunts routinely fail, with new research revealing that up to 30-40% of VP shunts fail within the first year of placement (1). Shunt obstruction is the most common cause of shunt failure (2). Our setting has one of the highest rates of shunt blockage (3,4). The reasons for our comparatively high failure rates in comparison to the Western world have yet to be determined. The ependymal lining, choroid plexus, or gliotic brain tissue in the proximal ventricular end can all block shunts. Kinking or disconnection of the shunt tubing can also cause catheters to become obstructed along the tract. Proteinaceous debris might clog the catheters' lumens as well. The omentum, adhesions, or pseudocysts are the most common causes of abdominal end blockage.

The typical cerebrospinal fluid (CSF) protein concentration is 0.2 to 0.4g/L. 10 High CSF protein concentrations are widely thought to

impede shunt function via a variety of ways (2). Despite the lack of strong data to support this practice, clinical practice avoids placing VP shunts in patients with increased CSF proteins in favor of alternative CSF diversion methods (5). These include the use of external ventricular drains or frequent ventricular taps, both of which are associated with a significant risk of infection and the associated morbidity and mortality. The aim of this study was to evaluate the biochemical and cellular properties of CSF in hydrocephalic patients undergoing ventriculoperitoneal shunting, as well as the impact of these CSF parameters on outcome.

Materials and methods

This was a prospective cohort study conducted at Kenyatta National Hospital in Kenya. Patients were enrolled in the research after undergoing VP shunt surgery for hydrocephalus. Data obtained upon recruiting included study identification, age, gender, residence, and the etiology of hydrocephalus. In addition, data on CSF biochemistry, including proteins and glucose, as well as cellularity, was extracted from patient files. It is routine practice in our setting to collect CSF during venticuloperitoneal shunt placement for biochemical and microscopic analysis. This is common practice in the hospital for people with hydrocephalus. The patients were split into two groups based on their baseline CSF biochemical and cellular properties: normal and abnormal.

Patients were subsequently followed up on in neurosurgical clinics for three months, at which time shunt function was evaluated. The data collection tool was utilized to screen for shunt failure, which included clinical signs and symptoms as well as imaging findings. Clinical signs of shunt obstruction included a bulging fontanelle, fluid collecting along the shunt tract, a reduced level of consciousness, agitation, abdominal pain, nausea, and vomiting. CSF pleocytosis in the presence of fever was utilized to establish a diagnosis of shunt infection. A CT scan imaging of the head was performed on patients with clinical signs of shunt failure to confirm the diagnosis. The duration of shunt survival, defined as the number of days from the insertion of the ventriculoperitoneal shunt to the diagnosis of shunt failure, and the etiology of shunt failure, defined as shunt blockage or shunt infection, were the primary outcomes of interest during this follow-up period. Mechanical causes of shunt failure such as shunt component breakage, kinking, disconnection, or migration were excluded from the study.

Results

Demographic Data

A total of 82 patients met the inclusion criteria and were enrolled into the study. There were 46 (56.1%) males and 36 (43.9%) females. The patients' ages ranged from 3 weeks to 10 years, with a mean of 15.5 months. The majority of the patients (78.04%) were under the age of one year (Figure 1).

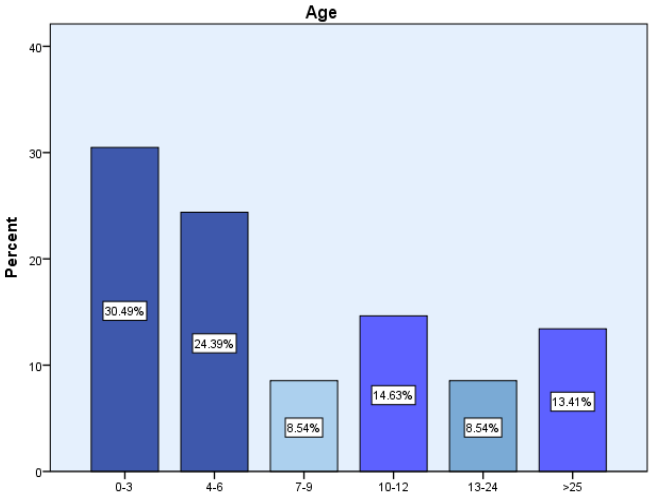

Figure 1: A bar chart illustrating the patient distribution by age

Etiology of Hydrocephalus

The etiology of hydrocephalus was determined by clinical history, laboratory tests and radiologic tests performed. Most of the patients had congenital hydrocephalus (82.9%). The commonest congenital intracranial malformation leading to hydrocephalus was Dandy walker malformation accounting for about 36.76% of all patients with congenital hydrocephalus

(Figure 2). Eighteen (21.9%) of the patients had spina bifida as well. The rest (78.1%) had hydrocephalus with no associated spinal neural tube defects

Type of surgery

The majority of patients, 76(92.7 %), underwent primary shunt placement, whereas 6(7.3 %) underwent shunt revision. The majority of shunt surgeries (96.3 %) were conducted by residents, the majority of whom were in their sixth year of residency (62.2 %). The rest were inserted by consultant neurosurgeon (3.6 %), fifth year residents (7.32%), and fourth year residents (30.49%).In all the patients in the study population, a medium pressure Chhabra shunt was used with the distal shunt catheter placed in the peritoneum.

Laboratory Findings

The majority of patients (52.44%) had normal CSF proteins, while the rest had increased CSF proteins. The reference range chosen was 150-400mMol/L. The mean CSF protein content was 588.3mMol/L (range from 5 to 2045mMol/L). Most of patients (65.9%) had low CSF glucose levels, with the mean CSF glucose content being 2.42mMol/L. The CSF cell count was normal in 86.6% of the patients. A cell count of more than 5 cells per high power field was regarded as abnormal.

Shunt failure

Eight (9.8%) of the patients had their shunts fail in the 3 month follow up period The average shunt survival for the shunts that failed was 60 days. Failure of all these shunts was attributed to shunt blockage.

Factors associated with Shunt Failure

Elevated CSF protein levels and decreased CSF glucose levels were significantly associated with shunt failure at 3 months (Table 1). Other variables investigated were not shown to be significantly related to shunt failure. Shunt failures were seen in all patients in this study who had increased CSF proteins or low CSF glucose. Shunt failure occurred on average 60 days after shunt placement in patients with increased proteins. At three months after insertion, 20% of the patients with increased CSF proteins had shunt failure, while only 2.3 percent of the patients with normal CSF proteins had shunt failure. According to the findings of this study, increased CSF proteins increase the risk of shunt failure by 8.7 times in the first three months after insertion.It was also observed that the protein concentration in individuals who experienced shunt failure was 1250mmol/L, compared to a mean protein concentration of 545mmol/L in patients whose shunts were functioning at 3 months.

The outcomes of the patients post recurrence were evaluated using the Eastern Cooperative Oncology Group (ECOG) / WHO/ Zubrod score. An outcome of 0-1 was defined as a good outcome, 2 as moderate outcome, 3 as severe outcome, 4 as vegetative state and 5 as death. The most frequent outcome was moderate at 38.89% (Figure 3).

Two patients died before intervention at recurrence. One patient presented with an infratentorial papillary adenocarcinoma whereas the other patient had a pineal gland tumor. The outcome of death was equal in both males and females and was significantly more if the tumor recurred within the first 6 months. Surgical intervention post recurrence resulted in patients having better outcomes relative to other patients who underwent other therapies.

Analysis of data

There was significant difference ($p = 0.047$) between age and outcome as assessed by Fisher-Freeman-Halton exact test. The significance tests carried out between the other variables were not significant. The results of the exact test are displayed in Table 1.

Table 1: Factors associated with shunt failure

		Shunt Failed		p-value
		No	Yes	
Gender	Female	30	6	0.062
	Male	44	2	
Etiology	Acquired	13	1	0.717
	Congenital	61	7	
Spina bifida	No	57	5	0.284
	Yes	15	3	
Type of Shunt Surgery	First	68	8	0.403
	Revision	6	0	
Resident year of training	Year 4	24	1	0.472
	Year 5	5	1	
	Year 6	45	6	
CSF proteins	Elevated	31	8	0.002
	Normal	43	0	
CSF Glucose	Abnormal	46	8	0.046
	Normal	28	0	
CSF Cellularity	Abnormal	9	2	0.311
	Normal	65	6	

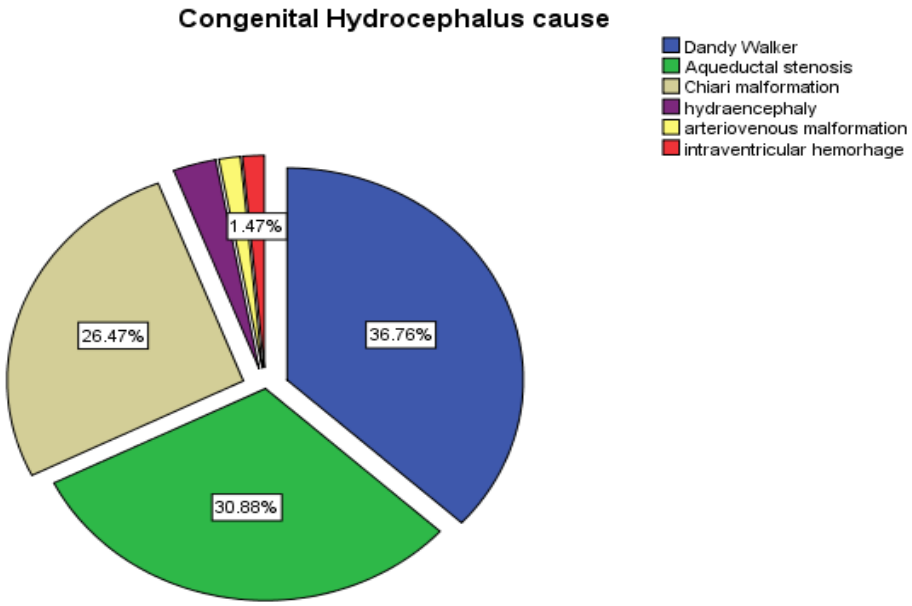

Figure 2: Frequency of various causes of congenital hydrocephalus in the study population

Discussion

Hydrocephalus remains a prevalent neurosurgical disorder in Kenya with more than 80 children treated in KNH in 2 months. Crude estimates of the prevalence of hydrocephalus in the East African region are between 0.47 to 0.60 per 100 live births with an estimated incidence of between 4900 and 8200 new cases per year in Kenya. This incidence is higher than that of sub-Saharan Africa which is estimated at 0.14 per 100 live births. From a global perspective, this is the highest incident rate reported with Latin America and North America reporting rates of 0.32 and 0.07 per 100 live births respectively (6).

There is an observed male predominance in the patients included in this study, with

46(56.1%) being male while 36(43.9%) of them were female. Kitunguu et al in 2017 reported a similar pattern of male predominance with 55.8% of the patients in his study being male. Previous studies in KNH by Noorani et al in 2003 and Omulo et al in 1993 have had similar findings as well (7). Worldwide, a similar observation has been made in most parts of the world except in Mozambique where the male to female ratio is 1:1.

As regards the radiologic investigation of children presenting with features of hydrocephalus, the majority (91.46%) of patients had cranial CT scan as the diagnostic imaging work up performed with only 4.8% of the patients having magnetic resonance imaging performed in the initial work up for hydrocephalus. Imaging tools available to the clinician in the initial assessment of hydrocephalic children include ultrasound, CT scans, and magnetic resonance imaging. The modality of choice in imaging pediatric hydrocephalus is MRI, as it provides detailed anatomical and functional information important in managing these patients (8). The reason most patients in this study underwent CT scan, which is not the gold standard imaging modality, is likely due to its wide availability, its relatively lower cost, and ease of performing in children without requiring sedation, compared to MRI.

Congenital hydrocephalus was the most common entity, diagnosed in 89.2% of the patients in this study with Dandy walker spectrum of malformations being the most identifiable congenital anomalies in 36.76% of those with congenital hydrocephalus. A similar finding was recorded by Omulo et al in the year 2000 in a study conducted in KNH with 74.4% of the patients he had studied having congenital hydrocephalus (9). Kitunguu et al in 2017 however had a different observation in a study conducted in the same institution, with a majority (57.1%) of the patients in his study having post-infectious hydrocephalus (10). This difference in etiology of hydrocephalus among patients managed in the same institution can be attributed partly to the different patient populations in each of the studies with the later study having included patients of all age groups while the former only studied pediatric hydrocephalus. Additionally, an earlier study in 1989 by Gichuhi et al on pediatric hydrocephalus in KNH found congenital hydrocephalus to be the commonest entity (9).

In the current study, 18(21.9%) of the patients had spina bifida. Of the these, 10 (55.5%) had elevated CSF protein while 8 (44.5%) had normal CSF proteins. There was no correlation between elevated CSF protein and the presence of spina bifida in this study. This variable could not be found in existing literature both locally and internationally. The presence of spina bifida did not affect shunt survival at 3 months in the present study.

For the large majority of patients in this study,76(92.7%) shunt surgery performed during the study period was the first-ever shunt insertion. This finding is in keeping with the findings of previous studies in the same institutions where primary shunt insertions account for 75-95% of children undergoing shunt surgery (7,9,11,12).

Most (96.3%) shunt surgeries in this study were performed by neurosurgery residents. D. Cochrane et al in 2005 reported that there is a relationship between the surgeon's operative experience and the shunt surgery outcomes with higher shunt failure rates at 6 months after surgery in less experienced surgeons (13). Anderson et al in 2021, in a prospective study, reported that the presence of a pediatric neurosurgeon during shunt surgery had better 30-day outcomes than surgeries performed by residents alone.39. In the current study, there was no statistically significant difference in 90-day outcomes between shunt outcomes performed by residents in different stages of their training. This finding is in keeping with that of a previous study conducted in the same institution in 2010 by the principal investigator in this study (11).

With regards to the CSF protein content, 52.4% of the patients had normal CSF proteins while 47.6% had elevated CSF

proteins. This variable could not be found in literature both locally and internationally for comparison. This is an important finding that highlights that nearly half of the patients undergoing shunt insertion for non-tumor hydrocephalus in our hospital have elevated CSF protein. It was further noted that elevated CSF proteins increase the likelihood of shunt failure in the first 3 months after insertion by 8.7 times.This study thus shows the impact that elevated CSF proteins have on shunt survival. Elevated CSF proteins has been reported to increase the likelihood of shunt failure due to shunt blockage in patients with tuberculous meningitis (5, 14). In an in vitro study established that the average incubation period to shunt blockage attributed to high CSF proteins was 46days (2). In this current study, the average incubation period was 60days. A study by Kitunguu et al (10) in the same institution showed that among the shunts that failed, the average incubation period was 67 days.

The overall shunt failure rate in this study was 9.8% at 3 months of follow-up. All shunt failures were attributed to shunt blockage. A previous prospective study in the same institution reported a shunt blockage rate of 10% (7). A retrospective study by Mwachaka et al in 2010 in the same institution reported that shunt blockage accounted for a majority (53.8%) of the shunt complications seen in KNH.

Nurhayat et al in a retrospective multicenter study noted that a persistently elevated CSF protein level above 100mg/dl was associated with shunt infection (11). No case of shunt infection was noted in this current study among the patients with elevated CSF proteins. Fulkerson et al, in his 10year retrospective cohort study on the risk factors for shunt failure in low-birth-weight preterm infants, observed a similar finding that there was no correlation between CSF protein levels and the risk of shunt infection (1).

With regards to CSF cellularity and shunt blockage, this study finds no correlation between elevated CSF cell count at shunt insertion and the likelihood of shunt failure at 3 months. A similar observation was made in neonates undergoing VP shunting after intraventricular hemorrhage and also in patients with tuberculous meningitis undergoing VP shunting (14).

There was a positive correlation between reduced CSF glucose and the risk of shunt failure at 3 months. studies in neonates with post hemorrhagic hydrocephalus (1) and with post tuberculous hydrocephalus (14) have had a contrary finding with both concluding that there was no link between CSF glucose level and shunt failure. It is also important to note that all patients with shunt failure at 3 months and low CSF glucose at shunt insertion also had elevated CSF proteins. The author here hypothesizes that partial treatment of preceding meningitis could explain this finding of reduced CSF glucose with elevated proteins. Further studies to validate this finding are therefore warranted.

Conclusion

Shunt blockage remains the leading cause of early shunt failure in KNH. About half of the pediatric patients undergoing ventriculoperitoneal shunting in KNH have elevated CSF proteins. Elevated CSF proteins or reduced CSF glucose at the time of surgery for shunt insertion were shown to increase the likelihood of shunt failure by 3 months of follow-up. We recommend closer follow up of patients with elevated CSF proteins of reduced CSF glucose at ventriculoperitoneal shunt insertion so as to screen for features of shunt failure. Further studies on the chemical interaction between shunt tubings and CSF proteins that leads to shunt blockage are also recommended. The findings of such a study can later inform the materials used to manufacture shunts that will have less interactions with CSF proteins.

Limitations and delimitations

This study provides the first ever description of common biochemical parameters in children with hydrocephalus, not only in Kenya but in the East African region. A longer duration of follow-up would have been better to screen for the effects of the CSF

biochemical and cellular characteristics over many years of follow-up. A larger patient group would have also yielded higher-quality data about this important neurosurgical disorder.

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