



Research Article

Patterns of Microbial Infections in Post-Infective Hydrocephalus and Treatment Methods at Bugando Medical Center

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Abstract

Background: Post Infective Hydrocephalus is among the complicated types of hydrocephalus and poses a challenge in management of these patients, globally. Antibiotics susceptibility patterns of common bacteria implicating in pyogenic ventriculitis complicated with hydrocephalus were not clearly known at our setting. Therefore, we determined antibiotics susceptibility patterns of common bacteria implicating in pyogenic ventriculitis complicated with hydrocephalus to recommend empirical therapy while waiting for culture and sensitivity results at Bugando Medical Centre (BMC) in Mwanza, Tanzania. **Methods:** Thirty-five patients with hydrocephalus who had undergone cerebrospinal fluid (CSF) tapping and analysis were selected randomly retrospectively and their bacteriological culture and sensitivity results were analyzed to determine the common microbial patterns. Patients were rationally prescribed antibiotics depending on laboratory results for 7 days and were later done control CSF cultures until negative cultures were achieved. **Results:** A total of 35 patients with median (interquartile range [IQR]) age was 5.5 [2-8] months were reviewed. The majority of participants were males, 62.9% (22/35). 20% (7/35) and 37.1% (13/35) had turbid CSF-shunt sample and first culture positive results, respectively, whereas one patient had culture positive with two pathogens resulting to 14 isolates. Gram positive bacteria were predominantly isolated (66.7%, 8/14), whereby *S. aureus* was frequently encountered (35.7%, 5/14). Overall, gram positive and negative bacteria exhibited least resistance against tetracycline (16.7% and 25%) and ciprofloxacin (16.7% and 25%) respectively. Three (8.6%) patients died from respiratory complications. **Conclusion:** Post infective hydrocephalus is a clinically challenging but treatable form of hydrocephalus and *Staphylococcus aureus* is the most common cause. This study found that the use of a seven-day regimen as cost effective and associated with a shorter hospital stay with the focus on CSF analysis with subsequent microbial targeted antibiotic therapy to achieve sterile CSF culture. Treatment strategy should be multidisciplinary approach with collaboration from microbiologists, radiologists, pediatricians and neurosurgeons.

Keywords

Post-Infective Hydrocephalus, Cerebral Spinal Fluid, Microbial Pattern, *Staphylococcus Aureus*

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1. Introduction

Hydrocephalus is defined as an increase in the fluid-containing spaces of the brain with increased pressure, resulting from an imbalance between CSF production and absorption or flow. This definition excludes other abnormalities of CSF dynamics, such as benign intracranial hypertension, in which the ventricles are not enlarged, and hydrocephalus ex vacuo, in which cerebral atrophy and focal destructive lesions lead to an abnormal increase of CSF passively.

Post-infective hydrocephalus (PIH) refers to accumulation of fluid within the cranial cavity (hydrocephalus) secondary to either pyogenic or tuberculous meningitis. Whereas in the former condition, fibrous adhesions develop in the ventricles and arachnoid villi, in the latter, the fibrosis is mainly basal.

Commonly patients present with varying symptoms varied such as increasing head size, hypo-activity, difficulty with swallowing, fontanelle fullness, vomiting, irritability, headaches and occasionally stupor [1].

The mainstay of treatment of hydrocephalus is ventriculoperitoneal shunt (VPS) surgery [2-4] and endoscopic third ventriculostomy (ETV) [5] has been selectively used with acceptable results.

In this article, we retrospectively review a series of 35 patients who were tested and treated for primary ventriculitis with further definitive treatment of postinfective hydrocephalus with VPS and review the published literature.

2. Materials and Methods

Study design, duration, population and setting

This was cross-sectional hospital based study conducted for one year from April 2019 to April 2020 where by 35 patients recruited who were admitted at Bugando medical center (BMC), with hydrocephalus condition and were treated by multidisciplinary team composed of neurosurgeons, pediatricians, radiologists and microbiologists. BMC is a consultant, teaching and zonal referral hospital for six regions around Lake Zone serving an estimated population of 13 million people. BMC has capacity of 1000 beds whereby about 500 children aged between 0-15 years with hydrocephalus are attended annually for treatment and follow-up of various etiological types of hydrocephalus, mostly congenital hydrocephalus and pyogenic/ post infective hydrocephalus.

Selection criteria and sample collection

Most patients presented with various symptoms like increasing head size, hypo-activity, difficulty in swallowing, fontanelle fullness, vomiting, irritability, headaches and occasionally stupor [1]. Patients with signs of infections like fever and convulsion. Samples for cerebrospinal fluid of (CSF-shunt) about 3-4 ml of CSF shunt sample were aseptically collected in EDTA vacutainer tubes by skilled neurosurgeon and brought to the laboratory by 30 minutes after collected. At CUHAS laboratory bacteriological culture and sensitivity done, Patients with positive culture results, antibi-

otics were prescribed according to the sensitivity test, for two weeks. After completion of antibiotics another sample of CSF-shunt samples were taken for the aim of ensuring complete recovery. Blood work up was done for all patients on an intention-to-treat basis.

Initial radiological investigation included brain ultrasound, which was followed by computed tomography (CT) incase ultrasound revealed loculated ventricles [6, 7], a finding which was frequent in most patients with chronic condition.

Laboratory Procedures

Isolation of implicating bacteria

Upon receipt in the laboratory, all specimens were registered in laboratory book and given acquisition numbers. Then, samples were examined macroscopically before being purposely inoculated in brain heart infusion (BHI) broth for a duration of 6 hours to increase the chance of bacterial isolations. After broths incubation of 6 hours, samples were inoculated on chocolate agar (CA), 5% sheep blood agar (BA) and MacConkey agar (MCA) plates. Except for CA plates which were incubated in candle jar, all other plates (BA and MCA) were aerobically incubated at 37°C for 48 hours however growth interpretation were done after every 24 hours.

Identification of isolated bacteria to species level

In house prepared biochemical identification tests were used to identify isolated bacteria to their possible species levels. Sugars fermentation, CO₂ production, sulfur production, indole production, motility, utilization of citrate as the sole source of carbon, production of urease and production of oxidase tests were used for gram negative bacteria. Whereby, catalase, coagulase, novobiocin, bacitracin, optochin and bile aesculin were used for gram positive bacteria.

Antibiotics susceptibility testing

Disc diffusion method was used for testing bacteria susceptibility patterns to different antibiotic discs. For gram negative bacteria, ampicillin, tetracycline, trimethoprim-sulfamethoxazole, gentamicin, ciprofloxacin, ceftriaxone and meropenem discs were tested whereby for gram positive bacteria, erythromycin, trimethoprim-sulfamethoxazole, gentamicin, ciprofloxacin, tetracycline and vancomycin discs were tested. Briefly, a suspension of test bacteria equivalent to 0.5 McFarland standard solution was inoculated on Muller Hinton agar (MHA) plate to make an evenly lawn on which antibiotic discs were seeded within 15 minutes. Plates were then incubated aerobically at 37°C for 24 hours. Zones of inhibitions were interpreted as per Clinical and Laboratory Standards Institute guidelines of 2018.

Laboratory quality control

E. coli ATCC and *S. aureus* ATCC were used as control organisms to quality control our laboratory procedures.

Statistical analysis

STATA software version 13.0 was used for data analysis. Percentages and fractions were used to present categorical data while median (interquartile range [IQR]) were used to

present continuous data. Logistic regression analysis was used to show association between outcome (infection) and variables (demographic and clinical data) whereby a p-value of <0.05 at 95% confidence interval was considered statistically significant.

Ethical considerations

Ethical clearance to publish these data was granted by the joint Catholic University of Health and Allied Sciences-Bugando (CUHAS-Bugando) and Bugando Medical Centre (BMC)-Research Ethics and Review Committee. Doctor's request forms were considered as written consent forms, therefore participants were not requested to sign in informed

consent forms.

3. Results

Participants' information

A total of 35 patients were enrolled during this study period whose median (interquartile range [IQR]) age was 5.5 [2-8] months. The majority of participants were males, 62.9% (22/35). During sampling; 17.1% (6/35) and 8.6% (3/35) of patients had fever and convulsion respectively (Table 1).

Table 1. Participants' related information.

Variables		Frequency (n/N)/median [IQR]	Percentages (%)
Median [IQR] age in months		5.5 [2-8]	-
Gender	Males	22	62.9
	Females	13	37.1
Fever during sampling	Yes	6	17.1
	No	29	82.9
History of convulsion	Yes	3	8.6
	No	32	91.4

Culture results and predictors of positive culture results

In the laboratory, 20% (7/35) and 37.1% (13/35) had turbid CSF-shunt sample and first culture positive results, respectively. One patient had positive culture with two bacteria species making a total of 14 isolated bacteria. No patient among those with positive results for the first culture had

positive results for the second culture. Gram positive bacteria made the majority (66.7%, 8/14) of isolated species of which *S. aureus* being the predominant (35.7%, 5/14), (Figure 1). Turbidity of CSF-shunt sample predicts positive culture results (OR [95%CI], p-value: 18 [1.84-176.56], $p=0.013$), (Table 2).

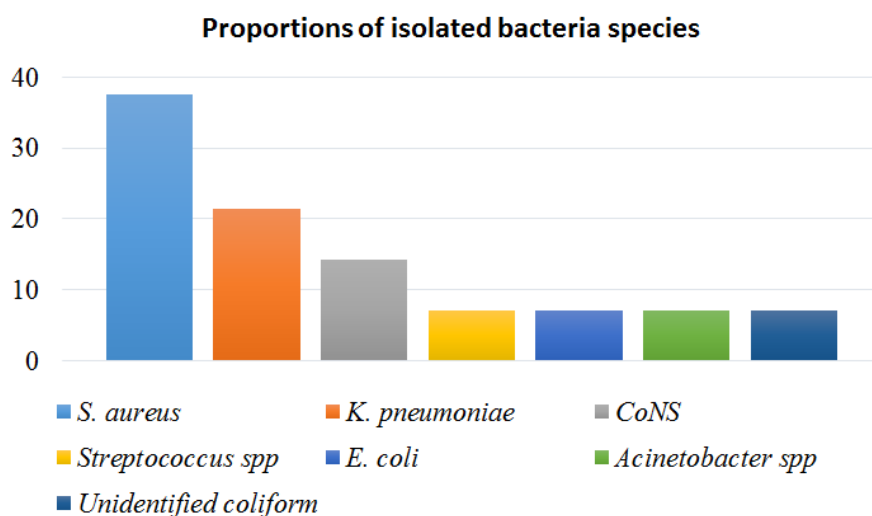


Figure 1. Proportions of isolated bacteria species from CSF-shunt samples.

Table 2. Predictors of positive culture results for CSF-shunt samples.

		Predictors of culture positive results				
Variables		Univariate analysis			Multivariate analysis	
		Negative	Positive	P value	OR [95%CI]	P value
Sample appearance	Clear	21 (75%)	7 (25%)	0.003	1	0.013
	Turbid	1 (14.3%)	6 (85.7%)		18 [1.84-176.56]	
Fever	No	17 (58.6%)	12 (41.4%)	0.254	1	0.276
	Yes	5 (83.3%)	1 (16.7%)		0.28 [0.03-2.74]	
Convulsion	No	19 (59.4%)	13 (40.6%)	0.164	-	-
	Yes	3 (100%)	0 (0%)		1	

Percentages resistance of isolated bacteria

Generally, percentage resistance of gram negative bacteria to ampicillin, trimethoprim-sulfamethoxazole, tetracycline, gentamicin, ciprofloxacin, ceftriaxone and meropenem was 100%, 100%, 16.7%, 33.3%, 16.7%, 83.3% and 0% respectively. On the other hand, percentage resistance of gram positive bacteria to trimethoprim-sulfamethoxazole, tetracycline, gentamicin, ciprofloxacin, erythromycin and vancomycin was 75%, 25%, 12.5%, 25%, 87.5% and 0% respectively.

Clinical Outcome and Follow up

In the postoperative period, 32 among the 35 patients recovered uneventfully and were discharged as soon as were clinically stable. 3 patients died due to respiratory complications were admitted to intensive care unit.

Patients were required to come for follow up after discharge six different visits at neurosurgery clinics scheduled visits were as follows at start 2 weeks after discharge then second visit after, one month, third visit after three months, four visit after six months then at one year which is the fifty visit and was considered as the last visit.

Put one paragraph explain more how you check for shunt complications what exactly you do One patient developed abdominal pseudocyst and was done laparotomy uneventfully, the second patient developed distal shunt blockage and was done revision successfully, whereas third patient developed hydrocele secondary to congenital hernia which was repaired.

4. Discussion

Postinfective hydrocephalus, (PIH) a complicated form of hydrocephalus associated with primary ventriculitis and obstructive hydrocephalus presents a socioeconomic and clinical burden to both the clinician and patient in terms of management and treatment owing to the inevitable cost of neuroimaging, long term use of antibiotics and eventual VPS

surgery/ ETV. Although no consensus in literary works has been concluded [5] on the causes and mechanism of microbial contamination, numerous studies have pointed to organism related infection being the most common cause of PIH [5, 8].

In a crosssectional study by Li and colleagues using polymerase chain reaction to determine bacterial 16S ribosomal DNA from CSF to determine if bacterial residua from recent infection, they found that Gram-negative bacteria in the phylum Proteobacteria were the most commonly identified [9] as opposed to our cohort in which Gram positive bacteria made the majority (66.7%, 8/14) of isolated species of which *S. aureus* being the predominant (35.7%, 5/14).

The plausibility that cross infection from mother to child as a possible cause of PIH was not supported in a survey of microbial spectrum of neonatal sepsis by Kiwanuka et al [10] with no concordance of bacteria recovered from blood and cerebrospinal fluid in addition to the important finding that Bacteria recovered from vaginal specimens were not resonant with those isolated from infants.

Other possible causes of PIH could include skin necrosis overlying the shunt system and shunt tract infection for patients with previous VPS treatment [4]. In a separate study by Kahamba et al [11] which objectively studied the patterns, causes and frequency of VPS complications, shunt infection was found to be the second most common shunt complication although the causative organisms were not explored.

Contrary to other studies, a large number of our patients did not present with meningeal irritation signs, a finding purportedly reported in similar studies [12]. however consistently presented with signs of increased intracranial pressure secondary to hydrocephalus secondary to non-communicating loculated-enlarged ventricles due to fibrous adhesions [7] within the ventricles as revealed on CT scan in most patients in our cohort. Paradoxically, most patients with PIH in our cohort did not present with fever, and as such

fever was not found to be statistically significant ($p=0.27$).

In our cohort, all patients were reviewed by pediatricians for comorbidities and the treatment strategy for PIV was multidimensional. Clinically, our drug specific antibiotic use for 7 days following culture and sensitivity results of CSF analysis, followed with control CSF studies which revealed sterility in 98% of our patients after 7 day regimen, consistent with our statistical findings in which no patient among those with positive results for the first culture had positive results for the second culture. In published scientific literature, the length of antibiotic use is still a matter of debate [13, 14].

From our findings, we found the use of a seven day regimen cost effective and associated with a shorter hospital stay in comparison with the four week use of antibiotics as advocated in most studies [8, 12, 14]. On that account, in LMICs setting we recommend for the use of a shorter organism-specific regimen with serial CSF analysis to minimize the overall cost of treatment and promote early rehabilitation.

In addition, patients symptomatic of active hydrocephalus requiring cerebrospinal fluid (CSF) diversion in whom immediate shunt surgery was not feasible were done external ventricular drains (EVD). An interesting feature in our study group was that ventricular tapping in 13 patients revealed yellowish pus which was non purulent, thick and at high pressure for which EVD placement was maintained until CSF became clear while being kept on antibiotics, a safe and efficient temporizing therapy as reported in similar studies [15]. In all patients, no cases were reported to have acquired ventriculitis associated with EVD as mentioned by other authors [16, 17]. Furthermore, all patients in our cohort were primary admissions with no previous history of long term hospital stay nor previous upper respiratory infections thence diasaffirming the notion of nosocomial infection [18] being a purported cause of PIH.

Subsequent control CT scan of brain revealed spontaneous clearance of fibrous membranes within the loculated ventricles with conversion into large communicating chambers hence paving way for an elective VPS surgery in resonance with studies by Chatterjee and colleagues [7].

In our study turbidity of CSF-shunt sample predicted positive culture results (OR [95%CI], p -value: 18 [1.84-176.56], $p=0.013$). These findings support the therapeutic use of ventricular tapping and eventual initiation of antibiotics for coverage of gram positive bacteria.

5. Conclusion

Conclusion: Post infective hydrocephalus is a clinically challenging but treatable form of hydrocephalus and *Staphylococcus aureus* is the most common cause in our setting. This study found that the use of a seven-day sensitive antibiotic regimen as cost effective and associated with a shorter hospital stay with the focus on CSF analysis with subsequent microbial targeted antibiotic therapy to achieve sterile CSF

culture. Treatment strategy should be multidisciplinary approach with collaboration from microbiologists, radiologists, pediatricians and neurosurgeons.

Abbreviations

BMC	Bugando Medical Center
CSF	Cerebrospinal Fluid
SI	Shunt Infection
PIH	Post-Infective Hydrocephalus

Conflicts of Interest

The authors declare no conflicts of interest.

References

- [1] James HE. Spectrum of the syndrome of the isolated fourth ventricle in posthemorrhagic hydrocephalus of the premature infant. *Pediatric neurosurgery*. 1990; 16(6): 305-8.
- [2] Mazzola CA, Choudhri AF, Auguste KI, Limbrick DD, Jr., Rogido M, Mitchell L, et al. Pediatric hydrocephalus: systematic literature review and evidence-based guidelines. Part 2: Management of posthemorrhagic hydrocephalus in premature infants. *Journal of neurosurgery Pediatrics*. 2014; 14 Suppl 1: 8-23.
- [3] Venkataramana NK, Mukundan CR. Evaluation of functional outcomes in congenital hydrocephalus. *Journal of pediatric neurosciences*. 2011; 6(1): 4-12.
- [4] Agarwal N, Shukla RM, Agarwal D, Gupta K, Luthra R, Gupta J, et al. Pediatric Ventriculoperitoneal Shunts and their Complications: An Analysis. *Journal of Indian Association of Pediatric Surgeons*. 2017; 22(3): 155-7.
- [5] Warf BC. Hydrocephalus in Uganda: the predominance of infectious origin and primary management with endoscopic third ventriculostomy. *Journal of neurosurgery*. 2005; 102(1 Suppl): 1-15.
- [6] Hubballah MY, Hoffman HJ. The isolated lateral ventricle. Experience at the Hospital for Sick Children. *Surgical neurology*. 1987; 27(3): 220-2.
- [7] Chatterjee S, Chatterjee U. Overview of post-infective hydrocephalus. *Child's nervous system: ChNS: official journal of the International Society for Pediatric Neurosurgery*. 2011; 27(10): 1693-8.
- [8] Harris L, Munakomi S. *Ventriculitis*. StatPearls. Treasure Island (FL) 2020.
- [9] Li L, Padhi A, Ranjeva SL, Donaldson SC, Warf BC, Mugamba J, et al. Association of bacteria with hydrocephalus in Ugandan infants. *Journal of neurosurgery Pediatrics*. 2011; 7(1): 73-87.
- [10] Kiwanuka J, Bazira J, Mwanga J, Tumusiime D, Nyesigire E, Lwanga N, et al. The microbial spectrum of neonatal sepsis in Uganda: recovery of culturable bacteria in mother-infant pairs. *PloS one*. 2013; 8(8): e72775.

- [11] Semali AKJKI. Complications of ventriculoperitoneal shunts in children in Dar es Salaam East and Central African Journal of Surgery 2005; 10(2): 55-9.
- [12] Lesourd A, Magne N, Soares A, Lemaitre C, Taha MK, Gueit I, et al. Primary bacterial ventriculitis in adults, an emergent diagnosis challenge: report of a meningococcal case and review of the literature. BMC infectious diseases. 2018; 18(1): 226.
- [13] Tokimura R, Iguchi M, Ito E, Murakami T, Ugawa Y. [The duration of antibiotic therapy in bacterial meningitis with pyogenic ventriculitis]. Rinsho shinkeigaku Clinical neurology. 2019; 59(3): 133-8.
- [14] Tunkel AR, Hasbun R, Bhimraj A, Byers K, Kaplan SL, Scheld WM, et al. 2017 Infectious Diseases Society of America's Clinical Practice Guidelines for Healthcare-Associated Ventriculitis and Meningitis. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2017; 64(6): e34-e65.
- [15] George T, Moorthy RK, Rajshekhar V. Long tunnel external ventricular drain: an adjunct in the management of patients with infection associated hydrocephalus. British journal of neurosurgery. 2019; 33(6): 659-63.
- [16] Ulloque-Caamano L, Mo-Carrascal J, Maraby J, Narvaez-Rojas A, Quintana-Pajaro L, Ramos-Villegas Y, et al. Ventriculitis associated with extraventricular drainage: etiology, diagnosis and treatment focused on neurocritical care units. Cirugia y cirujanos. 2019; 87(2): 230-40.
- [17] Dorresteijn K, Jellema K, van de Beek D, Brouwer MC. Factors and measures predicting external CSF drain-associated ventriculitis: A review and meta-analysis. Neurology. 2019; 93(22): 964-72.
- [18] Beer R, Lackner P, Pfausler B, Schmutzhard E. Nosocomial ventriculitis and meningitis in neurocritical care patients. Journal of neurology. 2008; 255(11): 1617-24.