



Ventriculoperitoneal Shunt Infection: A Study about Age as a Risk Factor in Hydrocephalus Pediatrics

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Abstract

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BACKGROUND: Shunt infection is one of the dreaded and serious complications following ventriculoperitoneal shunt (VP shunt) insertion, especially in a pediatric population. Numerous risk factors have been identified, particularly in developing countries, indicating that age may play an essential element in the pathogenesis of shunt infection, typically in patients <1-year-old. However, a few research demonstrate the inverse result.

AIM: The purpose of this was to determine the relationship between age and shunt infection so that it can be taken into consideration when performing VP shunt insertion.

METHODS: From January 2017 to December 2019, 98 pediatric patients with hydrocephalus who underwent VP shunt insertion were retrospectively reviewed to determine the relationship between age and shunt infection. We evaluated the microbiology results and management of shunt infection in patients with shunt infection.

RESULTS: Fifteen (15.15%) of 98 patients developed shunt infection. Patients aged >3–6 months had a significantly increased risk of shunt infection ($p = 0.04$; $RR = 4.15$; $CI\ 95\% = 1.19–14.45$). *Staphylococcus aureus* was the most frequently encountered pathogen in pediatric patients with shunt infection (53.3%), and the most common management for shunt infection was complete removal of the shunt and systemic antibiotics followed by re-insertion of the shunt after the cerebrospinal fluid was sterile (46.6%).

CONCLUSION: We conclude that age, especially those aged >3–6 months, has a significantly higher risk of shunt infection in pediatric patients.

Introduction

Management for pediatric hydrocephalus patients with ventriculoperitoneal shunt (VP shunt) insertion still has a high failure and complication rate [1], [2]. One of the most dreaded and serious complications following VP shunt is shunt infection [3]. Some studies report a varied incidence of shunt infection; there were 4.4% in Jakarta, Indonesia, 5.5% in Denmark, 15.5% in America, and 17.7% in Turkey [4], [5], [6], [7]. Pediatric patients tend to be more susceptible to shunt infections than adults, which can be caused by several factors, most commonly in patients <1-year-old, i.e., a perfectly underdeveloped immune system, premature age, exposure to potential pathogens, comorbid diseases, and other physiological factors [7], [8]. Another study, on the other hand, reports the opposite result. Braga et al. reported that patients over the age of 2 years are more vulnerable to infection [9], whereas other research found no correlation between age and shunt infection [10], [11].

Shunt infection has a wide impact on the patients, not only increasing morbidity and mortality

but also increasing costs associated with re-admission, procedures related to shunt infection, intravenous administration of antibiotics within a specified time period, and the new shunt system insertion, with an average treatment time of 7–21 days [12]. Thus, this study aimed to investigate whether there is a relation between the patient's age at the time of VP shunt insertion and shunt infection, especially in neurosurgery patients.

Methods

This was a retrospective cohort study (*historical cohort*) in which exposure and disease had occurred before the study's start. The variables of age risk factors during the placement VP shunt were measured through medical records.

Population and sample

From January 2017 until December 2019, this study included all pediatric patients with

hydrocephalus who have undergone VP shunt insertion at Dr. Sardjito General Hospital in Yogyakarta. The inclusion criteria were ≤ 18 years old, diagnosed with hydrocephalus confirmed by clinical and radiological examinations that had undergone VP shunt insertion with conventional shunt system, and had perioperative prophylactic antibiotics. While the exclusion criteria were post-infection hydrocephalus patients with the cerebrospinal fluid (CSF) analysis or bacteria culture result indicating positive growth of bacteria and patients with severe comorbid diseases (congenital heart disease, severe malnutrition, immune system disorders, congenital or systemic disorders that are severe and require further management).

Definition and criteria for infection

The criteria for shunt infection are at least one of the following criteria [13], [14]:

1. Positively found pathogenic microorganisms in CSF culture or shunt system with appropriate symptoms and signs of central nervous system infection or shunt malfunction; or
2. Surgical wound infection (wound breakdown/exposed shunt)/signs of infection along the shunt tract; or
3. Abdominal symptoms such as peritoneal infection or pseudocyst (even in the absence of culture-positive specimen).

Age as a risk factor

Evaluating age as a risk factor for shunt infection by determining and analyzing the age at VP shunt insertion that divided into four groups: < 3 months, more than 3 months but < 6 months, more than 6 months but < 12 months, and more than 12 months.

Analysis and ethics statement

The following data were collected, processed, and analyzed with univariate and bivariate using SPSS version 25.0 (IBM). This research has obtained ethical clearance approval from the Ethics Commission of the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, and a permit from Dr. Sardjito General Hospital with Reference Number: KE/FK/0950/EC/2019 and research permit from the Human Resources and Education Department of the Ministry of Health of the Republic of Indonesia, Directorate General of Health Services, Dr. Sardjito General Hospital number LB.02.01/XI.2.2/22807/2019.

Results

Patients characteristics

From January 2017 to December 2019, 98 patients were inserted VP shunt and were eligible as a research subject. All patients underwent surgery by a senior resident accompanied by a pediatric consultant neurosurgeon, utilizing a conventional shunt system; INA-Shunt semi-lunar flushing valve system with fixed pressure and VP shunt placement were performed at Keen's point. There were 55 males (56.1%) and 43 females (43.9%) with a minimum age of 14 days, a maximum of 18 years, and an average age of 5.47 years (± 4.97).

Incidence of shunt infection

Among 98 patients, there were 15 patients (15.1%) experienced shunt infection. Nine patients (60%) with a diagnosis of an exposed shunt, three patients (20%) with ventriculitis, one patient (6.6%) with ventriculitis + erythema lesion along the shunt tract, one patient (6.6%) with erythema lesion along the shunt tract and one patient (6.6%) with ventriculitis + abdominal problems (Figure 1).

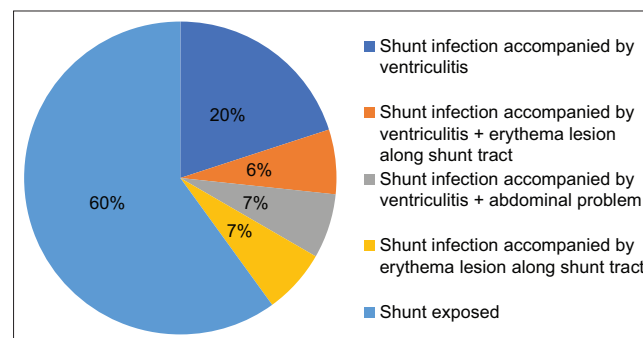


Figure 1: Shunt infection diagnosis

Age as risk factor

Analyzed by age, the highest shunt infection rate was $> 3-6$ months 4/13 (30.8%), followed by ≤ 3 months 6/23 (26.1%), $> 6-12$ months 1/8 (12.5%), and > 12 months 4/54 (7.4%). Age > 12 months as reference of the other range. This result found that patients age $> 3-6$ months are statistically significantly associated with an increased risk of shunt infection ($p = 0.04$) with RR = 4.15 which means patients with $> 3-6$ months are at risk of infection 4.15 times higher than age > 12 months, but age ≤ 3 months and $> 6-12$ months not significant (Table 1).

Microbiology examination

All patients with shunt infection patients are examined and identified for the pathogen collected

Table 1: Age as risk factor for shunt infection

Age	Infection				p	RR	CI 95%
	Yes		Not				
	n	%	n	%			
≤3 months	6	26.1	17	73.9	0.057	3.52	1.09–11.32
>3–6 months	4	30.8	9	69.2	0.040	4.15	1.19–14.45
>6–12 months	1	12.5	7	87.5	0.511	1.69	0.22–13.26
>12 months	4	7.4	50	92.6			

from the CSF, pus, or infected tissue/shunt device. The causative pathogens are represented in Table 2. The result shows several patients with monomicrobial and polymicrobial were isolated. Gram-positive bacteria were the predominant pathogen, and the rest were gram-negative bacteria, with the most common pathogen were *Staphylococcus aureus* (53.3%), *Staphylococcus epidermidis* (20%), and *Klebsiella pneumoniae* (20%).

Table 2: Profile of the causative pathogens

No	Characteristics	Results	
		Amount	Percentage
1	<i>Staphylococcus aureus</i>	8	53.3
2	<i>Staphylococcus epidermidis</i>	3	20.0
3	<i>Klebsiella pneumoniae</i>	3	20.0
4	<i>Coagulase vegative staphylococcus</i>	2	13.3
5	<i>Pseudomonas aeruginosa</i>	2	13.3
6	<i>Staphylococcus haemolyticus</i>	1	6.7
7	<i>Staphylococcus huminis</i>	1	6.7
8	<i>Citrobacter amalonaticus</i>	1	6.7
9	<i>Enterobacter cloacae</i>	1	6.7

Treatment of shunt infection

Of patients with shunt infection, four patients (26.6%) only underwent wound care along with topical and systemic antibiotics, three patients (20%) underwent shunt externalization and systemic antibiotics, which were then re-inserted after the CSF was sterile, seven patients (46.6%) underwent complete removal of the shunt and systemic antibiotics followed by re-insertion of the shunt after the CSF was sterile, and one patient (6.6%) died before the procedure (Figure 2). The most dominant antibiotic sensitive to cases of shunt infection were tetracycline 5 cases (7.1%), vancomycin 5 cases (7.1%), and trimethoprim-sulfamethoxazole 5 cases (7.1%).

Discussion

Age as risk factor

In the age factor for shunt infection, there was a relationship between the age at which the VP shunt was inserted and the incidence of shunt infection, with pediatric patients who had the VP shunt inserted when they were >3–6 months old tended to have shunt infection. Previous studies have reported that states that patients aged <1 year (12≤ months) will increase in the risk of shunt infection [15], [16], a finding that is

corroborated by other literature, which indicates that the rate of infection experienced by infants <6 months, generally had two to three times greater than adults [6]. Children who are <1 year old (≤12 months), especially those who are premature or have a low-birth-weight, are at very high risk of shunt infection. It is associated with a not fully developed humoral and cellular immune system, skin barrier protection that tends to be immature, changes in bacterial skin density, comorbidity, and other procedures [8], [15].

Interestingly, not similar to other results, we discovered that patients aged >3–6 months (4/13, 30.8%) tend to be more susceptible to infection than ≤3 months 6/23 (26.1%). Several theories were tried to explain this discovery. Because the newborn's acquired immune response is still forming, passive antibodies, such as maternal immunoglobulin G (IgG) antibodies, play a vital role in the neonate. Transplacental transfer of IgG from the mother to the fetus begins during the first trimester of pregnancy and can reach approximately 50% of the mother's IgG level at 30 weeks of gestation and increase to around 50% at 37–40 weeks of gestation, frequently exceeding the serum level in mothers delivering in term and healthy pregnancy [17], [18], [19], [20], [21], [22]. One of the IgGs obtained is IgG anti-Sa (*S. aureus*), which has been shown to improve neonatal resistance against *Staphylococcus* infection and is also supported by additional breastfeeding immediately after birth [23]. Another theory also mentions the presence of factors that modulate the immune response in neonates [24]. The neonatal serum contains a larger concentration of adenosine, an endogenous purine metabolite with immunomodulatory properties, and a higher basal ratio of interleukin-6 (IL-6)/tumor necrosis factor (TNF) than adults. Additionally, in response to toll-like receptor stimulation, monocytes from neonatal cord blood release a high ratio of IL-6 to TNF. By suppressing the inflammatory response and increasing microglial phagocytosis of *S. aureus*, the toll-like receptor can mediate a congenital immunological response to infection [25], [26], [27].

Microbiology examination

The most frequently encountered causal pathogen was *S. aureus* (53.3%), a gram-positive bacterium. *S. aureus* and *S. epidermidis* are normal skin flora bacteria that often cause shunt infection through the transmission of the skin, adhere to the implant's surface, and have biofilm-forming bacteria properties [15]. Although several attempts have been made to prevent intraoperative contamination by improving aseptic technique and limiting airborne transmission, the bacteria still dominate the cause of shunt infection. These results are in accordance with a previous report by Sacar *et al.*, who similarly reported high rates of infection with pathogen's patterns that tended to be the same [6].

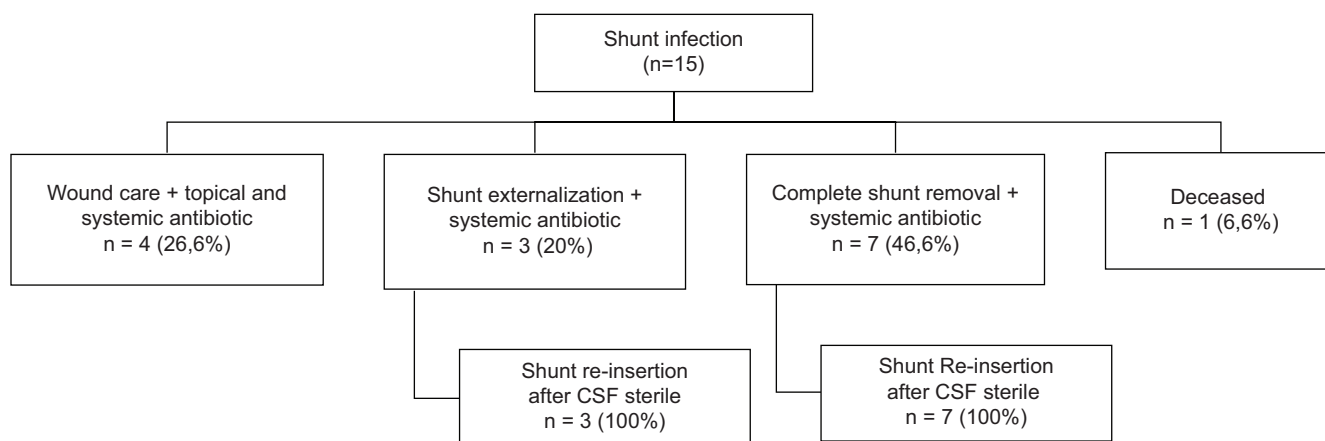


Figure 2: Treatment of shunt infection

This study also found the presence of shunt infections caused by gram-negative bacteria such as *K. pneumoniae* and *Pseudomonas aeruginosa*. High levels of gram-negative organisms allow the existence of simultaneous infections in the other part of the body that are responsible for the increased risk of morbidity and mortality. These results are in accordance with a previous report by Sacar *et al.* where gram-negative bacterial also dominate to be the cause of shunt infection [6]. This study also found some cases with clinical manifestation and symptoms of shunt infection, but with negative results or no pathogens growth, as conveyed by Fux *et al.*, where the diagnosis of cultures and *swabs* sometimes produces negative results due to the number of microorganisms attached to the surface of the shunt implant and only a small number of cells are found inside the planktonic state [28].

Treatment of shunt infection

Treatment for shunt infection is determined by the clinical condition of the patients and the doctor's preference. Some patients were only administered with antibiotics (topical and systemic) accompanied by debridement and wound care. Although the study reported by Walters *et al.* observed a higher mortality rate in shunt infection patients treated only just with antibiotics (37%) compared to those treated with antibiotics and surgery (17%), the cases faced in this study were shunt exposed without signs of systemic infection [29]. This is consistent with a study that determines the procedure for implant-related infections in neurosurgery patients can be determined based on the time of infection, wherein the case of acute infection (≤ 6 weeks) requiring wound debridement while maintaining the implant to remove necrotic tissue and mechanically reducing pathogen load on the implant layer surface, while accompanied by antibiotics [30]. In addition, if the shunt system is still functioning properly, antibiotic management can be combined with wound care/repair flap, and if there is

persistent infection following wound care/repair flap, shunt removal can be performed [31]. Some patients performed shunt externalization and complete shunt removal. Both groups were also given systemic antibiotics and re-insertion after the CSF was sterile. A systematic literature review study also provides level II recommendations on managing shunt infection by administering antibiotics along with shunt externalization or complete shunt removal [32].

Evaluation of antibiotic sensitivity found several dominant antibiotics were sensitive to the pathogen's pattern. The antibiotics vancomycin, tetracycline, and trimethoprim-sulfamethoxazole were the most dominantly sensitive. These findings can be considered options in determining prophylactic antibiotics and empirical antibiotics for the treatment of shunt infections. A meta-analysis study conducted that perioperative prophylactic antibiotics for 24–72 h after surgery can reduce the 50% risk of shunt infection. However, the function is less effective if the baseline infection is $\leq 5\%$ [33].

Conclusion

Throughout 2017-2019, the rate of shunt infection in Dr. Sardjito General Hospital was 15.15%. The patient's age $>3-6$ months at VP Shunt inserted is one of the risk factors that influence the incidence of shunt infection. Gram-positive bacteria became the predominant causative pathogen, with *S. aureus* (53.3%) being the most common among the isolates. The management of shunt infection varies greatly depending on clinical conditions and the evaluation of shunt system functions. Evaluation of CSF and shunt system removal are still the primary treatment accompanied by antibiotic administration until sterile CSF is obtained before the VP shunt re-insertion.

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