

# Evaluation of Pathogens in Shunt Infections Developed in Newborns Underwent Ventriculoperitoneal Shunt for Hydrocephaly

Hidrocefali Tanısı ile Ventriküloperitoneal Şant Takılan Yenidoğan Hastalarda Gelişen Şant Enfeksiyon Etkenlerinin Araştırılması

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## Abstract

**Amaç:** Ventriküloperitoneal (VP) şant, hidrocefali için en yaygın tedavi yöntemidir. Bununla birlikte, VP şant enfeksiyonu, yüksek mortalite ve morbidite oranları ile yaygın ve ciddi bir komplikasyondur. Bu çalışmanın amacı, hidrocefali nedeni ile takip edilen ve VP şant takılan neonatal hidrocefali olgularının klinik özellikleri, gelişen şant enfeksiyonları ve enfeksiyon etkenleri açısından değerlendirmektir.

**Gereç ve Yöntem:** Bu çalışma, retrospektif olarak, 2016 Ocak-2021 Haziran tarihleri arasında, 3. basamak bir hastane olan Harran Üniversitesi Tıp Fakültesi Yenidoğan Yoğun Bakım Ünitesi'nde gerçekleştirildi. Çalışmaya hidrocefali tanısı ile yatan ve VP şant takılan tüm yenidoğanlar dahil edildi.

**Bulgular:** Çalışmaya hidrocefali tanılı 52 olgu dahil edildi. Olguların 28'inde (%53,8) şant enfeksiyonu+menenjit gelişirken, olguların 24'ünde (%46,2) şant enfeksiyonu+menenjit gelişmedi. Şant enfeksiyonu+menenjit gelişen olguların 8 erkek (%28,6), 20 kız (%71,4) bebek olduğu görüldü. Kültürde üreme tespit edilen olguların 5'inde (%18) Gram-pozitif bakteriler ve 22'sinde (%78,4) Gram-negatif enterik ve non-fermenter bakteriler, 1'inde (%3,6) Candida parapsilozis saptandı.

**Sonuç:** Çalışmamızda Gram-negatif bakteriyel enfeksiyon insidansının yüksek olduğunu tespit ettik. VP şant enfeksiyonu düşünüldüğü durumlarda kültür sonucu çıkana kadar Gram-negatif etkenlere yönelik tedavi başlanmasının uygun olacağını düşünmekteyiz.

**Anahtar Kelimeler:** Hidrocefali, Şant Enfeksiyonu, Yenidoğan

## Öz

**Objectives:** The ventriculoperitoneal (VP) shunt is the most commonly used treatment modality in hydrocephaly. However, VP shunt infection is a common, severe complication with high mortality and morbidity rate. The aim of the study was to evaluate clinical characteristics, shunt infections and pathogen agents in newborns underwent VP shunt procedure for hydrocephaly.

**Materials and Methods:** This retrospective study was conducted in Neonatal Intensive Care Unit of Harran University, Faculty of Medicine between January, 2016 and June, 2021. The study included all newborns admitted with hydrocephaly and underwent VP shunt procedure.

**Results:** The study included 52 cases with hydrocephaly. Of the cases shunt infection plus meningitis was develop in 28 (53.8%) while no shunt infection plus meningitis was developed in 24 (46.2%). Of the cases developed shunt infection plus meningitis, 8 were boys (28.6%) and 20 were girls (71.4%). Of the cases with growth in culture tests, Gram-positive bacteria were detected in 5 (18.0%) whereas Gram-negative enteric and non-fermenter bacteria in 22 (78.4%) and Candida parapsilosis in one (3.6%).

**Conclusion:** In our study, we found that the incidence of Gram-negative bacterial infection was high. We believe that treatment with Gram-negative coverage will be appropriate until culture test results available when VP shunt infection is suspected.

**Key Words:** Hydrocephaly, Shunt Infection, Newborn

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## Introduction

Hydrocephaly is defined as accumulation of excessive cerebrospinal fluid (CSF) in ventricular and subarachnoid spaces, resulting in elevation in intracranial pressure (ICP). Although actual incidence of hydrocephaly is underestimated, congenital and infantile hydrocephaly incidence has been reported as 0.48-0.81: 1000 live birth (1). This incidence rate does not include hydrocephaly cases caused by intraventricular and subarachnoid hemorrhage, hypertension, elevated ICP, infections and tumors (1). Since prolonged elevation of ICP and dilated ventricles have deleterious effect on neuronal development, intervention to neonatal hydrocephaly is vital.

Currently, although it is not a radical treatment modality, shunt systems which ensures drainage of CSF to another body space in order to reduce ICP caused by intraventricular CSF accumulation are commonly used in the treatment of hydrocephaly (2). The goal of treatment is to identify how appropriate intraventricular pressure can be achieved. In addition, it is also important to decide optimal timing for shunting (3). The ventriculoperitoneal (VP) shunt-related complications include shunt obstruction, infection, excessive drainage and related clinical presentations. Shunt infection is one of the most important causes of shunt complications (4,5). VP shunt infections are an important problem with incidence of 5-15%, which hampers proper functioning of the shunt (6,7). Age is another factor that increase risk for shunt infection. Despite advanced surgical techniques, risk for shunt infection is higher in younger children (8,9). In conclusion, it is thought that VP shunt use in the treatment of hydrocephaly continues to lead infection despite advances in technology and novel measures (10).

In this study, it was aimed to evaluate clinical characteristics, shunt infections and pathogen agents in newborns underwent VP shunt procedure for hydrocephaly.

## Materials and Methods

This retrospective study was conducted in Neonatal Intensive Care Unit of Harran University, Faculty of Medicine between January, 2016 and June, 2021. The study included all newborns underwent VP shunt procedure with diagnosis of hydrocephaly.

The study was approved by Ethics Committee of Harran University, Faculty of Medicine (approval date: 14.09.2017; approval no: 09-10). The study was conducted in accordance to tenets of Helsinki Declaration. All data were retrospectively extracted from infection control committee records, patient files and electronic database. Fifty-two patients who applied with the diagnosis of hydrocephalus and underwent VP shunt were included in the study. All patients included were followed

during pre-operative and post-operative periods. It was shown that the patients were infection-free by clinical examination and laboratory studies before shunt procedure. In all patients, informed consent was obtained for anesthesia before surgery. The patients who had diagnosis of hydrocephaly but did not require shunt or had contraindication for shunt surgery were excluded. Patients who developed hydrocephalus secondary to intraventricular hemorrhage, Dandy-Walker syndrome, Arnold-Chiari malformation and other causes and had a shunt were included in the study.

The diagnosis of VP shunt infection was made by comprehensive clinical and laboratory evaluations. The CSF analysis was performed in the presence of criteria including irritability, recurrent fever, intolerance to feeding and convulsion. In patients with suspected shunt infection, CSF sample obtained from ventricle via direct puncture or from shunt reservoir was sent for CSF culture test. The patients with positive CSF culture were considered as VP shunt infection (11). In patients with suspected shunt infection, direct radiography and abdominal ultrasonography demonstrated radiologically that the shunt was in place. In addition, the shunts of the patients with shunt infection were removed and taken to external drainage. Control cultures were taken from the cases on days 14-21 of the treatment, considering the factors found in CSF cultures. The cases with sterile CSF culture results were consulted to the neurosurgery clinic. Antibiotherapy was completed to 21 days in patients with Gram-negative microorganism growth and 14 days in those with Gram-positive growth, and control cultures were stopped, as there was no growth.

### Blood and CSF Sampling for Culture Test and Analyses

CSF samples (2 mL) were obtained from ventricle via direct puncture or from shunt reservoir under aseptic settings. Blood samples (2 mL) were drawn from peripheral veins under aseptic settings. The blood and CSF samples were inoculated into Bactec Pds Plus/F media (Bactec Q 240, Bactec Dickinson). The passages from cases with growth were maintained in blood agar, EMB and chocolate agar. The antibiotic susceptibility was tested in Müller-Hinton Agar using Kirby-Bauer disk diffusion in accordance to Clinical Laboratory Standards Institute criteria (12). In addition, samples were also inoculated to Saboraud Dextrose Agar for fungal growth, which were incubated at 37 °C and assessed on hours 24 and 48. The antibiotic resistance and susceptibility were tested for all samples with growth.

In addition, for complete blood count, blood samples were also drawn into K2 EDTA (potassium-2-ethylene tetra acetic acid) tubes. The complete blood count was performed using Cell-Dyn Ruby analyzer (Abbott Diagnostics, Abbot Park, IL). The CRP was studied using Architect C16000 spectrophotometry analyzer (Abbott Diagnostics, Abbot Park, IL).

## Statistical Analysis

All statistical analyses were performed using SPSS version 24.0. Clinical characteristics were compared using demographic statistics. The data are presented as mean  $\pm$  standard deviation. Data were analyzed using descriptive statistics (frequency, mean, standard deviation). Mann-Whitney U test was used for binary comparisons while chi-square test was used to compare qualitative data. A p-value < 0.05 was considered as statistically significant.

## Results

Overall, 52 cases with diagnosis of hydrocephaly were included to the study between 2016 and 2021. When the cases were classified according to gestation age, it was found that 60.7% of cases were  $\leq$ 37-weeks old while 39.3% were >37-weeks old. Again, the birth weight was  $\leq$ 1500 g in 3.6%, 1500-2499 g in 25.0% and  $\geq$ 2500 g in 71.4%. Of the cases shunt infection was develop in 28 (53.8%) while no infection shunt was developed in 24 (46.2%). Of the cases developed shunt infection, 8 were boys (28.6%) and 20 were girls (71.4%) (Table 1). In cases with shunt infection, mean gestational age was  $36.64 \pm 2.24$  week and mean birth weight was  $2868 \pm 542.72$  gr (Table 1). In the CSF samples taken, the mean glucose value was 17.1 mg/dL, and the mean protein value was 660 mg/dL.

Of 28 cases with diagnosis of shunt infection, growth was detected in CSF culture test in 25 and in both CSF and blood culture tests in 17. Three patients with growth in blood culture and no growth in CSF culture were excluded from the study. The mean platelet value (MPV) and C-reactive protein (CRP) was significantly higher while mean hematocrit and hemoglobin values, mean corpuscular volume and plateletcrit were significantly lower in the shunt infection group (Table 2). No significant differences were detected in white blood cell, neutrophil, lymphocyte and MPV values between two groups (Table 2).

Among patients with diagnosis of shunt infection and growth in culture tests, Gram-positive bacteria were detected in 5 (18.0%) whereas Gram-negative enteric and non-fermenter bacteria in 22 (78.4%) and *Candida parapsilosis* in one (3.6%). *Klebsiella pneumoniae* was the most commonly isolated species in 13 patients (46.4%) (Table 3) (Figure 1).

## Discussion

VP shunt plays an important role in the management of hydrocephaly. However, shunt procedure is associated with many complications. Shunt failure may occur due to several mechanisms including obstruction, breakage, migration and infection. The shunt infection is the most common complication

**Table 1: Evaluations according to the demographic characteristics of the cases**

|                   | Shunt infection+meningitis (+)<br>(n=28) | Shunt infection+meningitis (-)<br>(n=24) | p-value |
|-------------------|--|--|---------|
|                   | Mean $\pm$ SD                            | Mean $\pm$ SD                            |         |
| Gestational age   | 36.64 $\pm$ 2.24                         | 36.79 $\pm$ 2.81                         | 0.83    |
| Sex               |  |  |         |
| Male              | 8 (28.6)                                 | 13 (54.2)                                | 0.9     |
| Female            | 20 (71.4)                                | 11 (45.8)                                |         |
| Birth weight (gr) | 2868 $\pm$ 542.72                        | 3056 $\pm$ 876.72                        | 0.35    |

**Table 2: Laboratory findings of the cases**

| Hematology (Unit)                | PA (n=28)           | Control (n=24)     | <sup>a</sup> p-value |
|----------------------------------|---------------------|--------------------|----------------------|
| WBC (10e3/uL) Mean $\pm$ SD      | 16.64 $\pm$ 7.32    | 17.13 $\pm$ 6.92   | 0.806                |
| NEU (10e3/uL) Mean $\pm$ SD      | 9.49 $\pm$ 5.34     | 7.59 $\pm$ 4.44    | 0.179                |
| LYM (10e3/uL) Median (min.-max.) | 5.52 $\pm$ 3.09     | 7.16 $\pm$ 5.21    | 0.178                |
| MPV (fL) Median (min.-max.)      | 7.17 $\pm$ 1.71     | 6.31 $\pm$ 1.32    | 0.053                |
| PLT (10e3/uL) Mean $\pm$ SD      | 424.07 $\pm$ 273.79 | 267.29 $\pm$ 98.29 | 0.010                |
| Hematocrit                       | 35.42 $\pm$ 8.46    | 50.83 $\pm$ 8.22   | 0.000                |
| Hemoglobin                       | 11.34 $\pm$ 2.55    | 17.26 $\pm$ 3.01   | 0.000                |
| MCV                              | 90.34 $\pm$ 10.24   | 101.45 $\pm$ 5.34  | 0.000                |
| PCT                              | 0.25 $\pm$ 0.13     | 0.16 $\pm$ 0.05    | 0.002                |
| CRP                              | 7.89 $\pm$ 7.70     | 0.1467 $\pm$ 0.26  | 0.000                |

SD: Standard deviation, WBC: White blood cell, PLT: Platelet, NEU: Neutrophil, LYM: Lymphocyte, MPV: Mean platelet volume, a: Independent samples t-test, MCV: Mean corpuscular volume; PCT: Plateletcrit, CRP: C-reactive protein

(13). Early diagnosis and appropriate management is an important aspect for shunt infection as it is a potentially life-threatening condition.

The shunt infections remain to be major source of medical problems leading adverse outcomes in children with hydrocephaly. Many efforts have been made to eliminate concerns regarding shunt infection. Pirotte et al. (14) prospectively adopted a strict sterile protocol for shunt implementation which does not involve use of antibiotic-soaked catheter or laminar air flow in order to reduce VP shunt infection rate. In the study, all procedures were performed same team including same senior surgeon, residence, nurse and an anesthesiologist. The sterile protocol was strictly applied to the team: surgical technique with sterile clothing, limited implant and skin manipulation, minimization of staff circulation in the room, scheduling as first surgery, prevention of CSF leakage, double gloves; procedure <30 min, systemic antibiotic prophylaxis (14).

To reduce VP shunt infection rate, Kestle et al. (15) used a similar, standardized protocol developed by 4 facilities from Hydrocephaly Clinical Research Network. Authors observed that

shunt infection rate decreased from 8.8% before implementation of protocol to 5.7% after protocol. However, shunt infections remain to be most important complication in the treatment of hydrocephaly.

In pediatric cases, age is one of the most important factors, which increases risk for VP shunt infection. The shunt insertion before 6 months of age has been considered as risk for shunt infection (16). In a study by Vinchon and Dhellemmes (16) it was found that the risk for VP shunt infection was increased by younger age. In the study including children aged <months and those aged >4 months, it was found that the risk for shunt infection was significantly increased in younger children. The risk for VP shunt infection was estimated as 5.6% in children aged >4 months while it was increased to 9.7% in children aged <4 months. It was reported that the infection rate was higher as age was decreased and that it was further increased in premature infants and those with low birth weight (16-19). In our study, we found that shunt infection rate was higher in neonatal age group (53.8%).

In the literature, it has been reported that prevalence of VP shunt infection is about 10% and it most frequently occurs within 2 months after surgery (16). In Turkey, VP shunt infection prevalence has been reported as 16%. The shunt infection-related mortality rate ranges from 10% to 13% (20,21). In a multi-center, retrospective study by Yakut et al. (22), 290 patients with VP shunt infection were reviewed and it was seen that VP shunt infection was developed in 121 patients (49.8%) within first month after surgery. Authors reported that the risk for shunt infection was higher within first few months after implementation (22). It was reported that 70% of shunt infections developed within first two months and only 10% of infections developed beyond one year (7,19,23). In a 6-years cohort study from Korea, it was found that 91.4% of VP shunt infection developed within first 3 months of shunt implementation (24). In studies from Turkey, it was reported that 71.4% of shunt infections developed within first 4 months after implementation whereas 49.8% developed after one year (19,22). In our study, it was seen that shunt infection developed in 53.8% of cases within first month after implementation in agreement with literature.

The most common pathogens are coagulase-negative staphylococci (member of normal skin flora) in VP shunt infection as *Staphylococcus epidermidis* and *Staphylococcus aureus* are being most commonly isolated microorganisms. Again, *Propionibacterium* spp. can also cause VP shunt infections. Besides Gram-positive bacteria, *Escherichia coli* and other Gram-positive are Gram-negative bacteria which may be involved in the etiology of shunt infections (25). Isla Guerrero et al. (26) reported that *S. epidermidis* was the most common pathogen

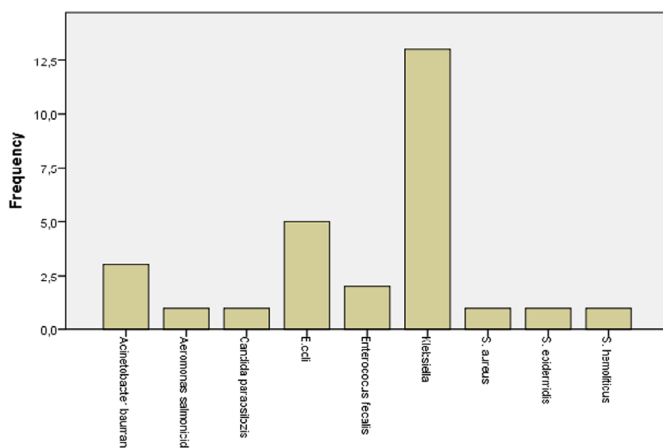


Figure 1: Distribution of reproducing agents in culture

| Table 3: Distribution of reproductive agents in CSF culture |           |              |
|---|-----------|--------------|
| Agents  | n         | %            |
| <i>Klebsiella</i>   | 13        | 46.4         |
| <i>E.coli</i>   | 5         | 17.9         |
| <i>Acinetobacter bauman</i>                                 | 3         | 10.7         |
| <i>Enterococcus faecalis</i>                                | 2         | 7.2          |
| <i>Aeromonas salmonicid</i>                                 | 1         | 3.6          |
| <i>Candida parapsilozis</i>                                 | 1         | 3.6          |
| <i>S. epidermidis</i>                                       | 1         | 3.6          |
| <i>S. aureus</i>  | 1         | 3.6          |
| <i>S. hemoliticus</i>                                       | 1         | 3.6          |
| <b>Total</b>  | <b>28</b> | <b>100.0</b> |

CSF: Cerebrospinal fluid

isolated in VP shunt infections. In another study, Parker et al. (27) found that *S. aureus* was the most common pathogen in shunt infections. In a multicenter study from Turkey, Yakut et al. (22) were able to isolate causative agent in 51% of cases. The most commonly isolated agent was coagulase-negative staphylococci by 42.5%; followed by *Pseudomonas aeruginosa* by 14.9%, *K. pneumoniae* in 10.1% and *S. aureus* in 10.1% (22). In our study, a microorganism was detected in CSF or blood culture test in 53.8% of cases and the most commonly isolated agents was *K. pneumoniae* (46.4%). In addition, we identified *E. faecalis* in 7.2%, *E. coli* in 17.9%, *S. epidermidis* in 3.6% and *S. aureus* in 3.6% of the cases.

Early diagnosis is highly important for mortality and morbidity in neonatal sepsis. In our study, white blood cell, neutrophil, lymphocyte, platelet, MPV and CRP levels were evaluated in newborns developed shunt infection. In a recent study by Lai et al. (28), it was reported that elevated serum CRP levels were more commonly observed in cases with Gram-negative etiology among patients with neonatal sepsis while Gram-positive coagulase negative staphylococci were more commonly isolated in cases with low CRP values. In a study by Gümüş and Kazanasmaz (29), elevated CRP levels were detected in 83.3% (n=50) and thrombocytopenia in 55.9% (n=33) of the cases with *K. pneumoniae* sepsis. In a study indicating a close relationship between Gram-negative sepsis and thrombocytopenia, Ree et al. (30) observed severe thrombocytopenia in 20% of septic newborns. In our study, *K. pneumoniae* was the most commonly isolated microorganism (46.4%). CRP and MPV values were found to be significantly higher in the group with shunt infection when compared to controls in our study. In a study by Makhoul et al. (31), elevated WBC count was detected in 40.9% of cases with Candida sepsis while leukocytosis or leukopenia favoring sepsis was detected in 59.1% of the cases with Candida sepsis. In our study, no significant differences were found regarding WBC, neutrophil or lymphocyte counts.

### Study Limitations

The most important limiting step of our study that it was made retrospectively. The second disadvantage is the risk of VP shunt. Control group to evaluate the factors is the absence.

### Conclusion

We found higher incidence of Gram-negative bacterial infection when compared to literature. Gram-negative pathogen growth was detected in 85.8% of the cases in our study. We think that higher incidence of Gram-negative bacteria in our population may be due to congenital malformation in majority of our patients and prolonged hospitalization. We believe that treatment with Gram-negative coverage will be appropriate

until culture test results available when VP shunt infection is suspected.

### Ethics

**Ethics Committee Approval:** The study was approved by Ethics Committee of Harran University, Faculty of Medicine (approval date: 14.09.2017; approval no: 09-10).

**Informed Consent:** In all patients, informed consent was obtained for anesthesia before surgery.

**Peer-reviewed:** Externally peer-reviewed.

### Authorship Contributions

Concept.; Design.; Data Collection or Processing.; Analysis or Interpretation.; Literature Search.; Writing: Both authors contributed equally.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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