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# " Antibiotic-impregnated and Nonantibiotic-impregnated ventriculoperitoneal shunts in Neonatal Myelomeningocele Associated with Hydrocephalus, Is there a valuable difference?"

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## ***Abstract:***

**Background:** Myelomeningocele (MMC) is a congenital defect of the central nervous system that inflicts a great burden on the patients and the healthcare system. Treatment of MMC involves placement of ventriculoperitoneal (VP) shunts for the associated hydrocephalus. The use of VP shunt is associated with potential complications such as shunt-related infections and shunt failures. The effectiveness of antibiotic-impregnated shunts to reduce the incidence of shunt infections is still debated.

**Objective:** This study aimed to compare the outcomes following insertion of antibiotic-impregnated versus nonantibiotic-impregnated ventricular and peritoneal shunts of the same type in cases of early postnatal surgical repair of myelomeningocele associated with hydrocephalus.

**Methods:** Neonates presented after antenatal or after birth diagnosis of MMC, associated with clinical and radiological evidence of hydrocephalus, who were scheduled for early surgical intervention within 48 h after birth were included. Those with mild hydrocephalus, and full-thickness skin covering the MMC sac that can be managed as elective surgery were excluded. During surgery, patients were to either managed with antibiotic-impregnated both ventricular and peritoneal (VP) shunt (Group A, N= 12), or nonantibiotic-impregnated VP shunt of the same type (Group B, N=13). In both groups, the incidence of shunt infection and wound dehiscence, the type of wound management, duration of antibiotic prophylaxis, the need for a secondary procedure, operative time, and hospital stay were assessed.

**Results:** The incidence of infection and partial wound dehiscence was non-significantly lower in group A than in group B (16.7% versus 30.8%, p=0.645). Two (16.7%) patients in group A required antibiotic use for more than 5 days compared with 4 (30.8%) patients in group B, with no significant difference (p=0.645). One patient in each group needed meticulous dressing and follow-up (8.3% versus 7.7%), whereas in between stitches and care was required in only 1 (8.3%) patient in group A compared with 3 (23.1%) patients in group B, with no significant difference. (p=0.787).

**Conclusions:** The findings indicate comparable outcomes of antibiotic-impregnated shunts compared to nonantibiotic-impregnated ones. Compared with AIS, non-AIS showed a non-significant reduction in shunt and CSF infection rates, which was noted with the use of AI systems.

**Keywords:** Myelomeningocele, hydrocephalus, neonates, antibiotic-impregnated shunts, infection rate

# INTRODUCTION

Myelomeningocele (MMC) is a congenital defect of the central nervous system characterized by protrusion of the meninges and spinal cord through open vertebral arches leaving the underlying neural tissue susceptible to damage. It is the most common and severe form of spina bifida that results from failure of neural tube closure during embryonic development genetic and micronutrient causes (Isaković et al., 2022).

Myelomeningocele inflicts a great burden on the patients and the healthcare system because it causes lifelong paralysis, various degrees of mental retardation, bowel and bladder dysfunction, and orthopedic disabilities, with a lifelong impact on the quality of life (Shobeiri et al., 2021)

Sonographic antenatal screening can detect MMC, however magnetic resonance imaging (MRI) is the diagnostic imaging tool that permits the diagnosis of spina bifida as early as the first trimester. Postnatal diagnosis depends on the clinical presentation of a midline defect and MRI findings of a cerebrospinal fluid-filled sac with a neural placode, which could be covered with meninges (Ushakov et al., 2019).

Myelomeningocele can be associated with other congenital disorders such as hydrocephalus and Chiari II malformation which represent the challenging clinical manifestations that carry significant complications in MMC. Hydrocephalus involves any enlargement of the cerebral ventricles and occurs in more than 85% of patients with MMC (Patel et al., 2020).

Treatment of MMC consisted of surgical closure of the spinal canal at birth as early as 72 hours after birth to reduce the risk of central nervous system infection and to improve outcomes, in addition to the lifelong supportive care (Alnaami and Alayad, 2019). Spina bifida patients require placement of ventriculoperitoneal (VP) shunts to prevent the neurologic and intellectual compromise that accompanies significant ventriculomegaly. The rate of shunt placement varies from 52% to 92% (Farmer et al., 2018). The use of VP shunt is associated with potential complications such as shunt-related infections and shunt failures. The development of infection results in prolonged hospital treatment, multiple surgeries, and reduced cognition and quality of life (Mnguni et al., 2020).

The effectiveness of antibiotic-impregnated shunts to reduce the incidence of shunt infections is still debated (Parker et al., 2015). This study aimed to compare the outcomes following insertion of antibiotic-impregnated versus nonantibiotic-impregnated ventricular and peritoneal shunts of the same type in cases of early postnatal surgical repair of myelomeningocele associated with hydrocephalus.

## METHODS

### Ethical considerations

This retrospective cohort study was approved by the Institutional Review Boards and the Ethical Committees of our University. Confidentiality of the patients' data was considered by assigning code numbers to the patients (known only by the researchers) and safe keeping of all patients' information

### Study design, settings, and duration

This retrospective cohort study included newly born infants with myelomeningocele and hydrocephalus who presented to our institutions between March 2018 and September 2021.

### Inclusion criteria

We enrolled neonates presenting after antenatal or after birth diagnosis of meningomyelocele (MMC), associated with clinical and radiological evidence of hydrocephalus and Evan's index (measured by a neuroradiologist) higher than 0.30 who were scheduled for early surgical intervention within 48 h after birth.

### Exclusion criteria

Neonates with mild hydrocephalus and MMC sac that can be managed as elective surgery were excluded.

### Preoperative assessment

The study participants underwent preoperative assessment including history taking, clinical examination, preoperative computed tomography (CT) scan of the brain and affected area of the spine was done. Magnetic resonance imaging of the brain and the whole spine was required for five patients to evaluate possible kinking of the cord in MMC sac and confirm trans-ependymal CSF permeation. Full routine laboratory investigations and echocardiography were also performed.

We collected data including maturity status at birth, birth weight, size and location of the MMC defect, preoperative Evan's index, timing in hours till surgery, and calculation of the MMC defect surface area.

## Operative technique

### *Preoperative preparation*

All patients born by cesarean section were admitted to the NICU and put were under meticulous evaluation by a pediatrician and an anthologist. Sterile dressing was applied and a systemic antibiotic combination of cefazolin (30 mg /kg via intravenous route) plus vancomycin(15 mg/kg intravenously) was immediately started.

### *Procedure*

The patient was placed in a prone position and surgical draping was done. Neurotoxic antiseptics that may cause damage to the neural placode were avoided. A skin incision close to the full thickness skin layer was done. Using a surgical microscope, splitting skin from the dura, and then separating the neural placode from the dura at the zona epitheliosa were done. The neural structure was fully released using intraoperative neurophysiological monitoring to protect neural tissues. Meticulous closure of the dura was done. Duragen was used in cases of wide dural defects (2 cases), one in each group, augmented by lumbar facia that was used as a second repair layer. The skin was closed primary with linear or multiple Z plasty skin closure.

The patient's position was then changed to a supine position to insert the ventricular and peritoneal (VP) shunt. High ICP was evaluated clinically and radiologically before shunt insertion. Shunts with median pressures were used. We used a combination of Metronic ARES® antibiotic-impregnated VP shunt tubes combined with valve system Mietheke pediGAV® 4/24 in 12 patients and non-antibiotic-impregnated VP shunts of the same type in another group of 13 patients. All the patients underwent standard ventriculoperitoneal shunt placement with a frontal Kocher's incision for a proximal catheter and a trans-rectus abdominal incision for a distal catheter.

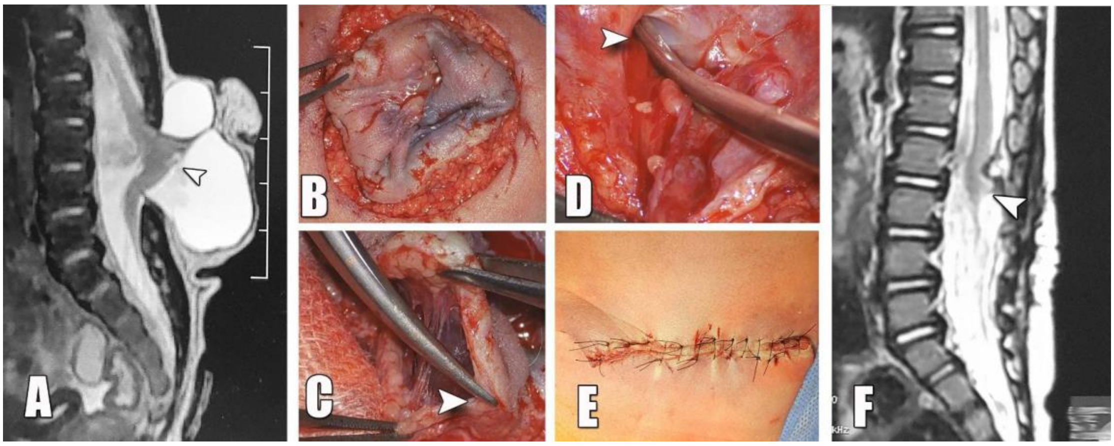


Fig 1 showing

A: MRI lumbosacral spine T2 mid-sagittal cut is showing myelomeningocele.

B, C, D, E images are showing surgical steps starting with dissection, repair and finally closure.

F: Postoperative MRI Lumbosacral spine revealed repaired myelomeningocele

***Postoperative care and follow up***

All patients were admitted to NICU for 5 days and were given the same antibiotic prophylaxis (vancomycin plus cefotaxime) for 5 days after surgery and more if needed. Meticulous wound care was done, avoiding pressure on incisions. Any wound dehiscence, CSF leak, or infection was carefully followed and treated.

After discharge, the follow-up visits were scheduled weekly for the first month and then monthly for six months to rule out an infection that could be related to the procedures. Shunt infection was suspected clinically by the presence of fever and erythema along the shunt track and then confirmed by laboratory investigations including cerebrospinal fluid sampling and a complete blood picture showing leucocytosis and further positive bacterial cultures. Postoperative Evan's index was measured, and CT brain was performed at 6 months following surgery. MRI lumbosacral spine was done for two cases post operatively.

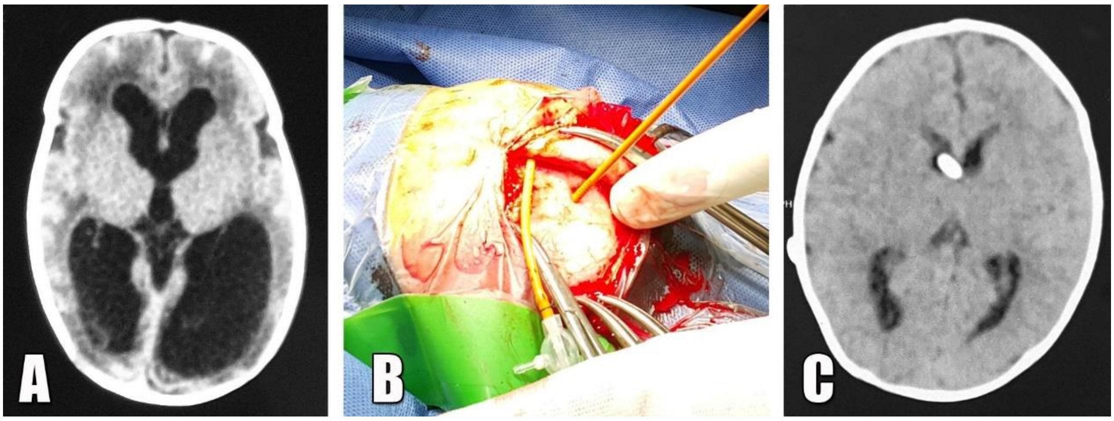


Figure 2 showing

A: CT brain of newly born male infant presented with hydrocephalic changes.

B: Insertion of ventricular catheter was done through Kocher's burr hole.

C: CT brain of the same infant postoperatively showed good insertion of ventricular catheter in the frontal horn of lateral ventricle.

**Outcomes**

During surgery, patients were to either managed with antibiotic-impregnated both ventricular and peritoneal (VP) shunt (Group A, N=12), or non-antibiotic-impregnated VP shunt of the same type (Group B, N=13). In both groups, the incidence of shunt infection and wound dehiscence, the type of wound management, duration of antibiotic prophylaxis, the need for a secondary procedure, operative time, and hospital stay were reported. Figures 1 and 2 demonstrate radiological images, surgical steps.

**Statistical analysis**

Data were analyzed using the Statistical Package for Social Science software, SPSS version 22. Qualitative data were presented as numbers and percentages and the association between 2 variables was tested by the Chi-Square test. Quantitative data were first tested for normality by the Shapiro Wilk test, and parametric data were summarized as mean ± standard deviation (SD) and were compared by the independent T-test. A p-value less than 0.05 was considered statistically significant.

## RESULTS

This study included 25 neonates who presented with MMC defect associated with hydrocephalus and were scheduled for early surgical intervention within 48 h after birth. During surgery, patients were managed with either antibiotic-impregnated both ventricular and peritoneal (VP) shunt (Group A, N=12) or non-antibiotic-impregnated VP shunt of the same type (Group B, N=13). All patients were followed-up for 6 months.

**Table 1** shows the preoperative data of the studied patients. Both groups showed homogenous sex and maturity distribution ($p>0.05$). The mean birth weight was 2908.3±541.8 g in group A and 2988.5±476.2 g in group B, with a nonsignificant difference ($p=0.698$). The locations of the defects in groups A and B were lumbar (41.7% versus 38.5%), lumbodorsal (25% versus 15.4%), and lumbosacral (33.3 versus 46.2), respectively, with no significant difference ($p=0.878$). The means of the defect size were 28.3±3.6 and 29.2±3.2 $cm^2$, respectively, with no significant difference ($p=0.512$). One (8.3%) patient in group A was associated with scoliosis compared with 2 (15.4%) patients in group B, with no significant difference ($p>0.999$). Two patients in group A were associated with other congenital anomalies including hydrocele or ventricular septal defect (8.3% each), while talipes equinovarus and undescended testis (7.7% each) were detected in two patients in group B, with no significant differences between both groups ($p>0.999$). The mean preoperative Evan's index was equal in both groups (0.33±0.01).

**Table 1. Preoperative data of the studied groups**

| | | Groups | | P-Value |
|---|---|---|---|---|
| | | Group A Antibiotic-impregnated shunt | Group B Non-antibiotic impregnated shunt | |
| Sex (N, %) | Female | 7 (58.3) | 7 (53.8) | 0.821 |
| | Male | 5 (41.7) | 6 (46.2) | |
| Maturity (N, %) | Full-term | 9 (75.0) | 11 (84.6) | 0.645 |
| | Preterm | 3 (25.0) | 2 (15.4) | |
| Birth weight in grams | Mean± SD | 2908.3±541.8 | 2988.5±476.2 | 0.698 |
| Location (N, %) | Lumbar | 5 (41.7) | 5 (38.5) | 0.878 |
| | lumbodorsal | 3 (25.0) | 2 (15.4) | |
| | lumbosacral | 4 (33.3) | 6 (46.2) | |
| Size of the defect ($cm^2$) | Mean± SD | 28.3±3.6 | 29.2±3.2 | 0.512 |
| Associated spinal anomaly (N, %) | Scoliosis | 1 (8.3) | 2 (15.4) | >0.999 |
| | Talipus equinovarus | 1 (8.3) | 0 (0) | |
| Associated congenital anomaly (N, %) | Hydrocele | 1 (8.3) | 0 (0) | >0.999 |
| | Talipes equinovarus | 0 (0) | 1 (7.7) | |
| | Undescended testis | 0 (0) | 1 (7.7) | |
| | Ventricular septal defect | 1 (8.3) | 1 (7.7) | |
| Preoperative Evan's index | Mean± SD | .33±.01 | .33±.01 | 0.989 |

N; number, SD; standard deviation

The mean time to surgery was comparable in both groups (30.3±9.9 in group A and 31.8±9.3 in group B, p=0.711). The mean operative time was non-significantly shorter in group A (135.4±10.1) than in group B (141.2±10.8), p=0.185. Additionally, the dura patch was used once in both groups (8.3% versus 7.7%, p>0.999) **(Table 2).**

**Table 2. Operative data of the studied groups**

| | | Groups | | P-Value |
|---|---|---|---|---|
| | | Group A Antibiotic-impregnated shunt | Group B Non-antibiotic impregnated shunt | |
| Time to surgery, hours | Mean± SD | 30.3±9.9 | 31.8±9.3 | 0.711 |
| Operative time, minutes | Mean± SD | 135.4±10.1 | 141.2±10.8 | 0.185 |
| Use of dura patch (N, %) | No | 11 (91.7) | 12 (92.3) | >0.999 |
| | Yes | 1 (8.3) | 1 (7.7) | |

N; number, SD; standard deviation

Regarding the outcomes in both groups, the incidence of infection and partial wound dehiscence was non-significantly lower in group A than in group B (16.7% versus 30.8%, p=0.645). The incidence of CSF infection was also non-significantly lower in group A than in group B (8.3% versus 23.1%, p=0.593). One patient in each group needed meticulous dressing and follow-up (8.3% versus 7.7%), whereas in between stitches and care was required in only 1 (8.3%) patient in group A compared with 3 (23.1%) patients in group B, with no significant difference. (p=0.787). Two (16.7%) patients in group A required antibiotic use for more than 5 days compared with 4 (30.8%) patients in group B, with no significant difference (p=0.645). Concerning the need for a secondary procedure, the shunt was obstructed, and surgical revision was done, with the restoration of the shunt function in one patient in group A. Correspondingly, one patient in group B has a shunt capsule exposed due to infection with wound disruption, and finally, the whole shunt was surgically removed **(Table 3).**

**Table 3. Postoperative outcomes in the studied groups**

| | | Groups | | P-Value |
|---|---|---|---|---|
| | | Group A Antibiotic-impregnated shunt | Group B Non-antibiotic impregnated shunt | |
| Incidence of infection | | 2 (16.7) | 4 (30.8) | 0.645 |
| Partial wound dehiscence | | 2 (16.7) | 4 (30.8) | 0.645 |
| CSF infection | | 1 (8.3) | 3 (23.1) | 0.593 |
| Wound care | In between stitches and care | 1 (8.3) | 3 (23.1) | 0.787 |
| | Meticulous dressing and follow up | 1 (8.3) | 1 (7.7) | |
| | Routine care | 10 (83.3) | 9 (69.2) | |
| Duration of antibiotics | 5 days | 10 (83.3) | 9 (69.2) | 0.645 |
| | More than 5 days | 2 (16.7) | 4 (30.8) | |
| Need for a secondary procedure | | 1 (8.3) | 1 (7.7) | >0.999 |
| Postoperative Evan's index (mean± SD) | | .29 ± .01 | .29 ± .01 | 0.492 |
| Hospital stay (mean± SD) | | 5.7±1.6 | 6.1±2.1 | 0.569 |

N; number, SD; standard deviation

## DISCUSSION

Insertion of drainage catheters for treating hydrocephalus associated with MMC is commonly complicated with infection. Ventriculitis or meningitis is a severe form of infection that can further deteriorate patients' conditions with high morbidity, mortality, and poor functional outcome (Karvouniaris et al., 2022).

Treatment of VP shunt infections involves hospital admission for the removal of the catheter and the placement of a temporary external ventricular drainage one, followed by the administration of systemic intravenous and/or intraventricular antibiotics (Schreffler et al., 2002).

The majority of shunt infections result from colonization of the device by microorganisms either from the skin flora or nosocomial pathogens acquired during surgery. Treatment of infection by antibiotics is challenged by the development of resistant pathogens and the difficulty of many important drug classes to penetrate the CSF and achieve therapeutic levels at the site of the infection. Furthermore, treatment of shunt infection is very costly. So, prevention of shunt infection is essential (Simon et al., 2019).

An antibiotic-impregnated shunt (AIS) was designed to reduce the rate of shunt infections, especially in the early postoperative period (Adams and Rajnik, 2014) but reports on their efficacy are conflicting.

The present study failed to find significant differences between AIS (group A) and non-AIS (group B) regarding the incidence of shunt or CSF infections, partial wound dehiscence, the need for meticulous dressing, and wound follow-up, and the duration of antibiotics use. The incidence of shunt infection and partial wound dehiscence was non-significantly lower in 16.7% in group A compared with (30.8%) in group B. The incidence of CSF infection was also non-significantly lower in group A than in group B (8.3% versus 23.1%, p=0.593). Furthermore, two (16.7%) patients in group A required antibiotic use for more than 5 days compared with 4 (30.8%) patients in group B, with no significant difference (p=0.645). Concerning the need for a secondary procedure, the shunt was obstructed, and surgical revision was done, with the restoration of the shunt function in one patient in group A. Correspondingly, one patient in group B has a shunt capsule exposed due to infection with wound disruption, and finally, the whole shunt was surgically removed. As well, the mean operative time was comparable in both groups.

In agreement with our findings, a retrospective study reviewed 160 shunts system and found no significant reduction in the pediatric CSF shunt infection rate with the use of AIS systems. The infection rate was 5.0% among patients with AIC compared with 8.8% in the control group (Kan and Kestle, 2007). In another single-center retrospective cohort study, AIS was associated with fewer early and late shunt infections (3.1%) than in the control group (15.2%), but there was no statistically significant difference (Aryan et al., 2005). Further, a single-blinded, randomized controlled trial, reported an absolute risk reduction in the shunt infection rate of 8.3% However, the results were not statistically significant because the study was of low power (Govender et al., 2003).

In contrast to our findings, several previous studies revealed significant efficacy of the AIS in reducing the incidence of infection. In their retrospective studya, Parker et al. (2009) reported significantly reduced rates of shunt infections in high-risk patients including premature infants that experienced meningitis or conversion of external ventricular drains, or stayed for a long time in the hospital. In a large multicenter study, AIS significantly reduced CSF infection rates in new and revision shunt implants (Kandasamy et al., 2011). The use of AIS significantly improved shunt infection rates in both children and infant populations with no evidence of increased antibiotic resistance (James et al., 2014).

The incidence of shunt infection and partial wound dehiscence was non-significantly reduced from 30.8% in non-AIS to 16.7% with the use of AIS, with a non-significant difference. In contrast, Raffa et al. (2015) reported a significant decrease in shunt infections from 34% to 9% in newborns and infants treated with a VP shunt for newly diagnosed hydrocephalus. The infection rate in our study agrees with the reported prevalence rates of shunt infection which varies from 1.5% to 69% (James and Bradley, 2008, Braga et al., 2009). Whereas, a multicenter study of 41 pediatric hospitals in the United States, reported a rate of CSF shunt infection ranging from 4.1% to 20.5% (Adams and Rajnik, 2014).

Analysis of a large nationwide administrative database to assess the incidence of infection for antibiotic-impregnated catheters versus standard shunt catheters revealed a significant reduction with the use of antibiotic-impregnated shunts both in adult and pediatric patients.

(Parker et al., 2015). Edwards et al. (2015) also demonstrated the cost-saving benefits of AIS insertion.

A recent randomized controlled trial provided valid evidence on the efficacy of AIS in reducing the infection rate compared with standard or silver shunts (Mallucci et al., 2020). A systematic review and meta-analysis assessed the efficiency of AIS in reducing the rate of shunt infection compared with standard shunts and demonstrated a significant reduction in the risk of shunt infection in pediatric patients (Qiu and Wu, 2020).

An earlier study by Kockro et al. (2000) evaluated AIS catheters with a scanning electron microscope and reported a reduction in the initial bacterial adherence and colonization to AIS catheters and further prevention of bacterial proliferation.

Lack of agreement of our findings with these studies might be due to inconsistent definition of a shunt infection between studies, presence of confounders for shunt infections such as age or prematurity, or extended hospital stay. Additionally, the small sample size is a limitation that might underpower our study. Further multicenter, blinded, randomized clinical trials recruiting very large patient numbers may provide more balanced information.

**Conclusions**

The findings in the present study indicate comparable outcomes of antibiotic-impregnated shunts compared to nonantibiotic-impregnated ones in cases of early postnatal surgical repair of myelomeningocele associated with hydrocephalus. Compared with AIS, non-AIS showed a non-significant reduction in shunt and CSF infection rates, which was noted with the use of AI systems. Additionally, partial wound dehiscence, the need for meticulous dressing and wound follow-up, the duration of antibiotics uses, and the need for a secondary intervention were similar in both groups. Up to our knowledge we can get similar results in both groups with perioperative antibiotics, good sterilization, shortening operative time and proper surgical tissue handing although further studies with large number of cases still needed to judge.

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