Neurosurgical Review (2025) 48:374
https://doi.org/10.1007/s10143-025-03521-1

RESEARCH

Impact of surgical timing and concomitant anomalies on neonatal meningomyelocele outcomes: a single-center experience

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Received: 17 October 2024 / Revised: 1 April 2025 / Accepted: 5 April 2025
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Abstract

To present a decade-long single-center experience with neonatal meningomyelocele (MMC) and to emphasize the impact of surgical timing and concomitant anomalies in these neonates. Neonates with MMC between 2012 and 2022 were retrospectively analyzed. Perinatal data, concomitant deformities and anomalies, maternal data, MMC repair surgery duration, concurrent surgeries, complications, and central nervous system (CNS) infection were evaluated. Outcome of 134 neonates with MMC is reported. Hydrocephalus was seen in 88 (65.7%), Chiari type II malformation in 84 (62.7%), orthopedic anomaly in 41 (30.6%), rib anomaly in 17 (12.7%), kyphosis in 26 (19.4%), and scoliosis in 5 (11.2%) neonates. 59 (44.0%) neonates underwent MMC surgery in < 48 h. Wound dehiscence/cerebrospinal fluid (CSF) discharge at the MMC repair site occurred in 5 (8.5%) neonates; only 2 (3.4%) had CNS infection. Late (> 48 h) repair was performed on 75 (55.9%) neonates. 6(8%) neonates experienced wound dehiscence/CSF discharge, and 8 (10.7%) developed CNS infection. Kyphectomy was performed on 9/26 (34.6%) neonates. Prognostic factors for kyphectomy included pregnancy number of MMC neonate ($p = 0.049$), postpartum MMC repair day ($p = 0.027$), number of previous operations ($p < 0.001$), presence and number of concurrent surgeries ($p < 0.001$ and $p < 0.001$, respectively), and history of Chiari II operation ($p = 0.002$). The prognosis for neonates with MMC is primarily determined by the effective surgical and medical management of associated deformities and conditions, such as kyphosis, hydrocephalus, and Chiari type II malformation, rather than the timing of MMC sac repair (early vs. delayed surgery). The decision-making process regarding the timing and technique of corrective surgeries should focus on the severity of symptoms related to Chiari II malformation and kyphosis in the neonate rather than their radiologic presence.

Keywords Chiari type II operation · Hydrocephalus · Neonatal kyphectomy · Neonatal meningomyelocele management

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Published online: 21 April 2025

Introduction

The neural tube develops early in embryonic life (around 28 days after conception), long before the mother is aware of her pregnancy, resulting in early brain and spine formation. Neural tube defects (NTDs) occur when the neural tube does not close entirely somewhere along its length, resulting in a hole in the spinal column or another type of anomaly [1]. The prevalence of NTDs varies based upon the type of pregnancy outcome (e.g., live birth, stillbirth, elective termination of pregnancy), as 0.5 per 1000 births. [2]. Furthermore, the rate changes significantly between countries where folic acid fortification is mandatory (0.3 per 1,000 births) and those where folic acid fortification is voluntary or non-existent (0.5 per 1,000 births). Geography is essential with prevalence being highest in Africa and Asia [2]. A systematic review and meta-analysis of countries with reliable birth defects surveillance programs showed that the average prevalence is reported as 1.9 cases per 1000 live births, with an uncertainty interval of 0.8–3.1 per 1000 live births [3]. According to numerous studies from Turkiye, this prevalence is 1.4–5.6 per 1,000 births [4, 5]. Genetic factors play an essential role in the recurrence of NTD in families. The risk of having NTD in siblings, second-degree relatives, and third-degree relatives of people with NTD is increased by 3.2%, 0.5%, and 0.17%, respectively. The risk increases to 10% when there are two siblings with NTD [6, 7].

Spina bifida is the most common type of spinal NTD, and it can be closed or open, depending on whether the defective tissues are covered with skin. Meningomyelocele (MMC) is the most common open spinal NTD [8]. Neonates with MMC are surgically treated, preferably during the first 48–72 h postpartum, to prevent central nervous system (CNS) infection and improve survival [9]. These neonates are at significant risk of developing CNS infection, and this risk increases if they undergo a ventriculoperitoneal shunt (VPS) surgery for accompanying hydrocephalus [10]. The risk of infection increases after the first 3 days of life [11].

MMC management is a complex multidisciplinary task. Multiple surgeries are expected after the first closure to best address the following conditions: hydrocephalus, Chiari II malformation, tethered cord, and concomitant organ anomalies and limb defects [12]. Hydrocephalus is decompressed via a VPS or an endoscopic third ventriculostomy [13]. Immediate surgery (within the first 48 h) and concomitant shunt placement are strongly recommended as the best treatment for these patients [14]. The vast majority of neonates with MMC have Chiari type II malformation associated with hydrocephalus. The displacement of the cerebellum, medulla, and fourth ventricle via the foramen magnum necessitates immediate surgical decompression of the posterior fossa structures and the prevention of subsequent hydrocephalus [15].

Scoliosis and kyphosis are two of the most common progressive spinal deformities in neonates with MMC. While both deformities are most prevalent in the lumbar area, scoliosis occurs in the upper and mid-lumbar levels, and kyphosis occurs in the lower thoracic and upper lumbar levels [16, 17]. Kyphosis is known to occur in 8%–20% of neonates with MMC, and severity changes according to the neurological segments it affects; higher lesions are at increased risk [18–21]. Studies on the surgical management of spinal deformities in children with MMC show that concurrent surgeries may be performed safely with tolerable outcomes. The concurrent approach is recommended because it results in shorter operation times, less blood loss, a longer temporary hospital stay, and better deformity repair [22, 23]. This study presents the surgical outcome and decade-long single clinical experience of 134 neonates with MMC and accompanying congenital anomalies.

Materials and method

A total of 140 neonates with MMC who were surgically treated and their mothers at our hospital between January 2012 and December 2022 were retrospectively analyzed. Patients with incomplete or unavailable data at our institutional patient medical record database system were not invited into this study. Of the 140 neonates, 4 were excluded from the study due to missing data because they were dropped out follow-up after the MMC operation, and 2 were excluded from the study due to their ruptured MMC at birth. The remaining 134 neonates were included in this study (Fig. 1).

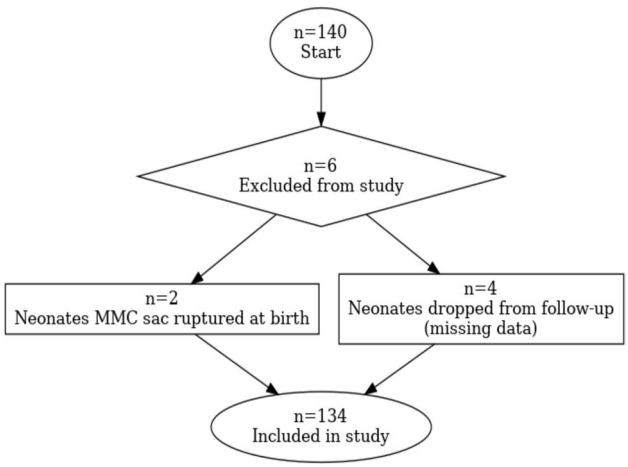


Fig. 1 Study population flow chart

Perinatal data (sex, birth weight [g], length [cm], head circumference [cm], and body mass index [BMI, kg/m^2], gestational age), concomitant deformities (hydrocephalus, Chiari type II malformation, scoliosis, and kyphosis) and anomalies (orthopedic and rib), neurologic status, maternal data (age and the number of pregnancy in which MMC neonate is delivered), MMC repair operation time, shunt operation time, concurrent surgeries (Chiari malformation correction and kyphectomy), the presence of wound dehiscence/CSF discharge and CNS infection, duration of hospital stay, and neonatal exitus were evaluated. CNS infection in this study was defined explicitly as infections occurring from the time of birth until the neonate's discharge from initial hospitalization following MMC repair and all necessary additional procedures.

All neonates in this study were followed up preoperatively (covers the period from the neonate's delivery, admission to the neonatal intensive care unit (NICU), and surgical consultation at the NICU to the time of MMC closure operations) and postoperatively. Informed written parental consent was obtained for each neonate for observation and participation in the study. Neonates with an open sac are not included in this study. Each neonate with a closed sac received appropriate antibiotic treatment following the clinical protocol (ampicillin 100 mg/kg/dose, 3 × 1/day, intravenous plus cefotaxime 100 mg/kg/dose, 3 × 1/day, intravenous) of our hospital, which was continued for 24 h after the operation [24, 25]. All the neonates were scanned with cranial and spinal magnetic resonance imaging before the correction surgery. The bony structures were evaluated with further spinal CT and 3D spinal CT. Neonates with hydrocephalus were decompressed by the VPS or an endoscopic third ventriculostomy (ETV).

Neonates with symptoms otherwise considered related to Chiari type II malformation: apnea, respiratory distress, persistent vomiting, poor feeding/feeding inability, and progressive weakness in the upper extremity underwent Chiari type II operation. The presence and severity of the clinical symptoms related to Chiari type II in the third cervical vertebra and below indicated the decision to corrective operation. The surgical techniques used for Chiari type II operations were cervical laminectomy, duraplasty, and/or occipital craniectomy [26].

Neonates with kyphosis were considered for kyphectomy to prevent progression and to improve function. Other indications were reducing respiratory impairment, increasing intraabdominal space, and managing associated pain. Neonates with a kyphotic angle larger than 50 degrees were operated [27]. During all the operations mentioned in this study, utmost care is provided for the surgical hemostasis of delicate neonates; therefore, perioperative blood transfusions were not required.

The study protocol was approved by the Ethics Committee of University of Health Sciences, Izmir Tepecik Training and Research Hospital (Protocol Number: 2022/12–11). This retrospective study was conducted in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Statistical analysis

The variables were analyzed using the SPSS 25.0 program (IBM Corporation, Armonk, NY). The data conformity to normal distribution was evaluated using the Shapiro–Wilk test and the variance homogeneity was assessed using Levene's test. Quantitative variables were compared between two independent groups using the Mann–Whitney *U* test with the Monte Carlo method and the independent samples *t*-test with bootstrap results. The Wilcoxon signed-rank test was used to compare the dependent variables. The Monte Carlo simulation approach was used to compare categorical variables, along with the Pearson chi-square, Fisher's exact, and Fisher–Freeman–Halton tests. The relationship between the categorical dependent variable and the explanatory variables was analyzed using logistic regression with the backward elimination method. The inclusion of variables in the model was determined based on the results of univariate analyses conducted with the dependent variable. Variables with p-values less than 0.10 were included in the initial model. The backward elimination method was preferred to optimize the number of variables included and improve the model's accuracy. The inclusion and exclusion criteria were set at $p < 0.05$ and $p > 0.10$, respectively. Cramér's w and Cohen's d effect sizes were included to quantify the strength of associations and measure the practical significance of the results. In the tables, quantitative variables are expressed as mean (standard deviation) and median (minimum–maximum), and categorical variables are expressed as *n* (%). Variables were analyzed at a 95% confidence level, and a *p*-value < 0.05 was considered significant.

Results

This study included 134 neonates with MMC, four of whom died during the follow-up period. 68 (50.7%) neonates were female, and 66 (49.3%) were male. Their median length was 48 cm, median head circumference was 35 cm, median body weight was 3,035 g, and median BMI was 24.44 kg/cm2, 131 neonates included in the study were delivered at term, the median gestational age was 38 weeks. Three were preterm, delivered at 35–35 and 37 weeks, respectively. These neonates were operated ≥ 48 h because of their necessity

Table 1 Descriptive statistics for the neonates in the study group

	n (%)
Wound Dehiscence/CSF Discharge at MMC site	
No	123 (91.8)
Yes	11 (8.2)
Central Nervous System Infection	
No	124 (92.5)
Yes	10 (7.5)
Gender	
Female	68 (50.7)
Male	66 (49.3)
Concurrent surgeries	
MMC	51 (38.1)
MMC + Shunt	71 (53)
MMC + Kyphectomy	1 (0.7)
MMC + Shunt + Kyphectomy	3 (2.2)
MMC + Shunt + Chiari	3 (2.2)
MMC + Shunt + Kyphectomy + Chiari	5 (3.7)
Shunt operation	
No	52 (38.8)
Yes	82 (61.2)
Kyphectomy	
No	125 (93.3)
Yes	9 (6.7)
Chiari Operation	
No	126 (94)
Yes	8 (6)
Hydrocephalus	
No	46 (34.3)
Yes	88 (65.7)
Chiari II malformation	
No	50 (37.3)
Yes	84 (62.7)
Orthopedic Anomaly	
No	93 (69.4)
Yes	41 (30.6)
Rib Anomaly	
No	117 (87.3)
Yes	17 (12.7)
Kyphosis	
No	110 (82.1)
Yes	26 (19.4)
Scoliosis	
No	119 (88.8)
Yes	15 (11.2)
Neurologic status	
Paraplegic	69 (51.5)
Paraparetic	28 (20.9)
Normal	37 (27.6)
Newborn Exitus	
Alive	130 (97)
Ex	4 (3)

Table 1 (continued)

	n (%)	
	mean (SD.)	**median (min-Q1-Q3-max)**
Length (cm)	47.54 (3.01)	48 (38–46–50–55)
Head circumference (cm)	35.63 (3.42)	35 (30–34–36.5–56)
Body weight (gr)	3076.99 (516.89)	3035 (1730–2800 - 3360–5030)
BMI (child)	24.45 (4.3)	24.44 (15.84–22.07–26.82–39.89)
Maternal age	28.03 (6.56)	27.5 (17–22–33–44)
In which pregnancy is MMC	2.74 (1.67)	2 (1–2–4–11)
Postpartum MMC operation day	4.31 (4.07)	3 (0–1–6–20)
Number of operations	1.74 (0.71)	2 (1–1–2–4)
Postpartum shunt operation day	9.48 (11.64)	7 (0–0–15–74)
Duration of hospitalization (day)	28.42 (22.64)	22 (2–15–35–158)
Gestational age	38. (0.51)	38 (35–38 - 38–39)

SD Standard deviation, *min* minimum,
Q1: Percentile 25, Q3: Percentile 75, max: Maximum
MMC Meningomyelocele, *Ex* Exitus

for adequate alimentation to increase their BMI appropriate for the operation.

None of the neonates in this study had an open (ruptured) sac. With a high danger of contamination and the emergence of a central nervous system infection (CNSI), this condition is a surgical emergency. Until CNSI is under control, additional corrective procedures for hydrocephalus and Chiari type II abnormality cannot be carried out in neonates with ruptured MMC [28, 29]. Two neonates with ruptured MMC sacs were consulted at the NICU between January 2012 and December 2022, but these neonates were not included in this study. The median maternal age was 27.5 years. When women gave birth to a neonate with MMC, they were in their median second pregnancy.

All neonates were operated on with parental informed consent. The median day of MMC surgery was 3 days after delivery. Each neonate had a median of 2 operations. Shunt procedures were performed at a median of 7 days after birth, with a median hospitalization duration of 22 days (Table 1).

MMC surgical repair was performed within 48 h in 59 (44.0%) neonates. Wound dehiscence/CSF discharge at the MMC repair site occurred in 5 (8.5%) neonates, with only 2 (3.4%) neonates developing CNS infection. Hydrocephalus was seen in 40 (67.8%), Chiari type II malformation in 32 (54.2%), an orthopedic anomaly in 18 (30.5%), rib anomaly in 8 (13.6%), kyphosis in 13 (22.0%), and scoliosis in 10 (16.9%) neonates. MMC repair was performed on 20 (33.9%) neonates, shunt surgery on 39 (66.1%), kyphectomy on 2 (3.4%), and Chiari surgery on one (1.7%) neonate (Table 2). The neurologic outcomes of the neonates were paraplegic in 29 (49.2%), paraparetic in 17 (28.8%), and normal in 13 (22.0%). The paraplegic neonates also had paraplegia before the correction surgeries. Two (3.4%) neonates died during the follow-up, and the median hospitalization duration was 22 days (Table 2). The first of the neonates died due to the development of necrotizing enterocolitis during follow-up. In the other neonate, sudden death of an unknown cause occurred on the second day following the surgery.

In contrast, surgical repair of MMC was performed > 48 h in 75 (55.9%) neonates. Wound dehiscence/CSF discharge at the MMC repair site occurred in 6 (8.0%) neonates, and 8 (10.7%) neonates had CNS infection. Hydrocephalus was seen in 48 (64.0%), Chiari type II malformation in 52 (69.3%), orthopedic anomaly in 23 (30.7%), rib anomaly in 9 (12.0%), kyphosis in 13 (17.3%), and scoliosis in 5 (6.6%) neonates. MMC repair was performed on 31 (41.3%) neonates, shunt surgery on 43 (57.3%), kyphectomy on 7 (9.3%), and Chiari surgery on 7 (9.3%) in this group.

The neurologic outcomes of the neonates were paraplegic in 40 (53.3%), paraparetic in 11 (14.7%), and normal in 22 (32.0%). Two (2.7%) neonates died during the follow-up, and the median hospitalization duration was 23 days (Table 2). The first of the neonates died due to neonatal sepsis on the 6th postoperative day, and the other died due to urosepsis on the 5th postoperative month.

In our series, neonates with rib anomaly (95% confidence interval [CI] 0.103–0.241, $p = 0.034$) and scoliosis (95% confidence interval [CI] 0.125–0.266, $p = 0.021$; Table 3) moderately tended to wound dehiscence/CSF discharge at the MMC operation site. Neonates with scoliosis suffered 4.99 more times of wound dehiscence/CSF discharge (OR 4.999, 95% CI 1.163–21.481, $p = 0.031$; Table 7).

Table 2 Prognostic factors in early and late interventional MMC repair operations and prognostic factors for CNS infection in early and late MMC repair operations

	Timing of MMC Repair Operation		*p*	Timing of MMC Repair Operation (> 48 h)		*p*	Effect Size [95% CI]
	≤ 48 h (*n* = 59)	> 48 h (*n* = 75)		CNSI (No) (*n* = 67)	CNSI (Yes) (*n* = 8)		
Wound Dehiscence/CSF Discharge at MMC site $_{n\ (\%)}$	5 (8.5)	6 (8)	0.999[f]	6 (9)	0 (0)	0.999[f]	
Central Nervous System Infection, $_{n\ (\%)}$	2 (3.4)	8 (10.7)	0.185[f]	-	-	-	
Gender (Male), $_{n\ (\%)}$	27 (45.8)	39 (52)	0.492[c]	35 (52.2)	4 (50)	0.999[f]	
Length (cm), $_{mean\ (SD.)}$	47.51 (2.87)	47.57 (3.13)	0.912[t]	47.62 (3.19)	47.13 (2.7)	0.642[t]	
Head circumference (cm), $_{median\ (min/max)}$	35 (30/56)	35 (31/43)	0.924[u]	34.5 (31/43)	37.5 (35/43)	**0.004**[u]	1.236[d] [0.476/1.995]
Body weight (gr), $_{mean\ (SD.)}$	3109.86 (559.89)	3051.12 (482.65)	0.516[t]	3022.03 (477.06)	3294.75 (490.8)	0.110[t]	
BMI (child), $_{mean\ (SD.)}$	24.48 (4.42)	24.43 (4.23)	0.951[t]	24.63 (4.3)	22.74 (3.38)	0.138[t]	
Maternal age, $_{median\ (min/max)}$	28 (17/43)	27 (17/44)	0.267[u]	27 (17/44)	28 (24/37)	0.397[u]	
In which pregnancy is MMC, $_{median\ (min/max)}$	3 (1/11)	2 (1/8)	0.053[u]	2 (1/8)	3.5 (2/4)	**0.025**[u]	0.580[d] [0.159/1.319]
Number of operations, $_{median\ (min/max)}$	2 (1/4)	2 (1/4)	0.868[u]	2 (1/4)	2 (1/4)	0.370[u]	
Concurrent surgeries, $_{n\ (\%)}$			0.237[ff]			0.581[ff]	
MMC	20 (33.9)	31 (41.3)		29 (43.3)	2 (25)		
MMC + Shunt	37 (62.7)	34 (45.3)		29 (43.3)	5 (62.5)		
MMC + Kyphectomy	0 (0)	1 (1.3)		1 (1.5)	0 (0)		
MMC + Shunt + Kyphectomy	1 (1.7)	2 (2.7)		2 (3)	0 (0)		
MMC + Shunt + Chiari	0 (0)	3 (4)		3 (4.5)	0 (0)		
MMC + Shunt + Kyphectomy + Chiari	1 (1.7)	4 (5.3)		3 (4.5)	1 (12.5)		
Shunt operation, $_{n\ (\%)}$	39 (66.1)	43 (57.3)	0.372[c]	37 (55.2)	6 (75)	0.454[f]	
Kyphectomy, $_{n\ (\%)}$	2 (3.4)	7 (9.3)	0.298[f]	6 (9)	1 (12.5)	0.562[f]	
Chiari Operation, $_{n\ (\%)}$	1 (1.7)	7 (9.3)	0.078[f]	6 (9)	1 (12.5)	0.562[f]	
Hydrocephaly, $_{n\ (\%)}$	40 (67.8)	48 (64)	0.715[c]	42 (62.7)	6 (75)	0.703[f]	
Chiari II malformation, $_{n\ (\%)}$	32 (54.2)	52 (69.3)	0.105[c]	44 (65.7)	8 (100)	0.097[f]	
Postpartum shunt operation day, $_{median\ (min/max)}$	6 (0/74)	9 (0/43)	0.620[u]	9 (0/42)	9.5 (0/43)	0.589[u]	
Orthopedic anomaly, $_{n\ (\%)}$	18 (30.5)	23 (30.7)	0.999[c]	21 (31.3)	2 (25)	0.999[f]	
Rib anomaly, $_{n\ (\%)}$	8 (13.6)	9 (12)	0.800[c]	9 (13.4)	0 (0)	0.585[f]	
Kyphosis, $_{n\ (\%)}$	13 (22.0)	13 (17.3)	0.517[c]	10(14.9)	3 (37.5)	0.136[f]	
Scoliosis, $_{n\ (\%)}$	10 (16.9)	5 (6.7)	0.096[c]	5 (7.5)	0 (0)	0.999[f]	
Neurologic status, $_{n\ (\%)}$			0.104[c]			0.072[ff]	
Paraplegic	29 (49.2)	40 (53.3)		34 (50.7)	6 (75)		
Paraparetic	17 (28.8)	11 (14.7)		9 (13.4)	2 (25)		
Normal	13 (22)	24 (32)		24 (35.8)	0 (0)		
Newborn exitus (Exitus), $_{n\ (\%)}$	2 (3.4)	2 (2.7)	0.999[f]	2 (3)	0 (0)	0.999[f]	
Duration of hospitalization (day), $_{median\ (min/max)}$	22 (2/103)	23 (4/158)	0.414[u]	22 (4/158)	45.5 (27/109)	**< 0.001**[u]	1.113[d] [0.358/1.867]
Gestational age, $_{median\ (min/max)}$	38 (38/39)	38 (35/39)	0.347[u]	38 (35/39)	38 (38/39)	0.999[u]	

[f]Fisher Exact Test (Monte Carlo), [c]Pearson Chi-Square Test (Monte Carlo), [t]Independent Samples T Test (Bootstrap), [ff]Fisher Freeman Halton Test (Monte Carlo), [u]Mann Whitney U Test (Monte Carlo), SD.: Standard Deviation, min: Minimum, max: Maximum

Duration of hospitalization strongly correlated with wound dehiscence/CSF discharge (95% confidence interval [CI] 0.479–1.741, $p = 0.001$; Table 3). This trend was also significant when analyzed with multivariate logistic regression analysis (OR 1.028, 95% CI 1.007–1.049, $p = 0.009$; Table 7). Male neonates (95% confidence interval [CI] 0.103–0.330, $p = 0.032$) with scoliosis (95% confidence interval [CI] 0.095–0.345, $p = 0.044$) who underwent concurrent MMC closure and shunt operation had significant would dehiscence/CSF discharge at the operation site, resulting in a longer duration of hospitalization (95% confidence interval [CI] 0.304–2.020, $p = 0.009$; Table 4). The multivariate logistic regression analysis also supported this trend. Scoliotic neonates with MMC closure and shunt operation had 8.72 times increased wound dehiscence/CSF discharge at the operation site (OR 8.728, 95% CI 1.251–60.892, $p = 0.029$). Longer duration of hospitalization was also significant in concurrent MMC closure and shunt operations in

Table 3 Prognostic factors for wound dehiscence/CSF discharge at MMC operation site and CNS infection

	Wound Dehiscence/CSF Discharge at MMC site		*p*	Central Nervous System Infection		*p*
	No (*n* = 123)	Yes (*n* = 11)		No (*n* = 124)	Yes (*n* = 10)	
Gender (Male), $_{n\ (\%)}$	63 (51.2)	3 (27.3)	0.207[c]	62 (50)	4 (40)	0.745[f]
Height (cm), $_{median\ (min/max)}$	48 (38/55)	48 (43/54)	0.760[u]	48 (38/55)	47.5 (43/50)	0.440[u]
Head circumference (cm), $_{median\ (min/max)}$	35 (30/56)	34.5 (33/40.5)	0.562[u]	35 (30/56)	37.5 (34/43)	**0.008[u]**
Body Weight (gr), $_{mean\ (SD.)}$	3073.11 (514.64)	3120.36 (565.65)	0.767[t]	3062.81 (521.44)	3252.8 (441.85)	0.151[t]
BMI (Infant), $_{mean\ (SD.)}$	24.35 (4.24)	25.61 (5.02)	0.363[t]	24.58 (4.35)	22.89 (3.34)	0.123[t]
Maternal age, $_{median\ (min/max)}$	27 (17/44)	30 (20/36)	0.955[u]	27 (17/44)	28 (20/37)	0.641[u]
In which pregnancy is MMC, $_{median\ (min/max)}$	2 (1/11)	3 (1/4)	0.881[u]	2 (1/11)	3 (1/4)	0.250[u]
Postpartum MMC operation day, $_{median\ (min/max)}$	3 (0/20)	4 (0/12)	0.994[u]	3 (0/20)	4.5 (0/15)	0.622[u]
Number of operations, $_{median\ (min/max)}$	2 (1/4)	2 (1/4)	0.281[u]	2 (1/4)	2 (1/4)	0.252[u]
Concurrent surgeries, $_{n\ (\%)}$			0.342[ff]			0.440[ff]
MMC	48 (39)	3 (27.3)		49 (39.5)	2 (20)	
MMC + Shunt	65 (52.8)	6 (54.5)		64 (51.6)	7 (70)	
MMC + Kyphectomy	1 (0.8)	0 (0)		1 (0.8)	0 (0)	
MMC + Chiari	0 (0)	0 (0)		0 (0)	0 (0)	
MMC + Shunt + Kyphectomy	3 (2.4)	0 (0)		3 (2.4)	0 (0)	
MMC + Shunt + Chiari	2 (1.6)	1 (9.1)		3 (2.4)	0 (0)	
MMC + Kyphectomy + Chiari	0 (0)	0 (0)		0 (0)	0 (0)	
MMC + Shunt + Kyphectomy + Chiari	4 (3.3)	1 (9.1)		4 (3.2)	1 (10)	
Shunt operation, $_{n\ (\%)}$	74 (60.2)	8 (72.7)	0.528[f]	74 (59.7)	8 (80)	0.315[f]
Kyphectomy $_{n\ (\%)}$	8 (6.5)	1 (9.1)	0.549[f]	8 (6.5)	1 (10)	0.514[f]
Chiari operation, $_{n\ (\%)}$	6 (4.9)	2 (18.2)	0.131[f]	7 (5.6)	1 (10)	0.472[f]
Hydrocephalus, $_{n\ (\%)}$	80 (65)	8 (72.7)	0.748[f]	80 (64.5)	8 (80)	0.493[f]
Chiari II malformation, $_{n\ (\%)}$	77 (62.6)	7 (63.6)	0.999[f]	75 (60.5)	9 (90)	0.090[f]
Postpartum Shunt Operation Day, $_{median\ (min/max)}$	7 (0/74)	12 (0/38)	0.164[u]	7 (0/74)	7.5 (0/43)	0.589[u]
Orthopedic anomaly, $_{n\ (\%)}$	36 (29.3)	5 (45.5)	0.311[f]	38 (30.6)	3 (30)	0.999[f]
Rib anomaly, $_{n\ (\%)}$	13 (10.6)	4 (36.4)	**0.034[f]**	17 (13.7)	0 (0)	0.361[f]
Kyphosis, $_{n\ (\%)}$	23 (18.7)	3 (27.3)	0.446[f]	23 (18.5)	3 (30)	0.407[f]
Scoliosis, $_{n\ (\%)}$	11 (8.9)	4 (36.4)	**0.021[f]**	15 (12.1)	0 (0)	0.602[f]
Neurological status, $_{n\ (\%)}$			0.280[ff]			0.463[ff]
Paraplegic	61 (49.6)	8 (72.7)		62 (50)	7 (70)	
Paraparetic	26 (21.1)	2 (18.2)		26 (21)	2 (20)	
Normal	36 (29.3)	1 (9.1)		36 (29)	1 (10)	
Newborn Exitus (Ex), $_{n\ (\%)}$	3 (2.4)	1 (9.1)	0.293[f]	4 (3.2)	0 (0)	0.999[f]
Duration of hospitalization (Day), $_{median\ (min/max)}$	22 (2/109)	42 (11/158)	**0.001[u]**	22 (2/158)	38.5 (13/109)	**0.015[u]**

[c]Pearson Chi-Square Test (Monte Carlo), [u]Mann Whitney U Test (Monte Carlo), [t]Independent Sample T Test (Bootstrap), [ff]Fisher Freeman Halton Test (Monte Carlo), [f]Fisher Exact Test (Monte Carlo), SD.: Standard deviation, min: Minimum, max: Maximum

which the neonate developed wound dehiscence/CSF discharge at the operation site. (OR 1.03, 95% CI 1.004–1056, $p = 0.0.024$; Table 7).

In the group, when the MMC repair procedure was performed beyond 48 h, neonates with rib anomaly (95% confidence interval [CI] 0.144–0.395, $p = 0.020$) and scoliosis (95% confidence interval [CI] 0.074–0.359, $p = 0.048$) were moderately more prone to develop wound dehiscence/CSF discharge at the operation site. Overall, the major determiner of the wound dehiscence/CSF discharge at the operation site was the duration of hospitalization (95% confidence interval [CI] 0.628–2.364, $p = 0.030$; Table 5). According to multiple regression analysis, scoliotic neonates who operated in ≥ 48 h developed 11 times more wound dehiscence/CSF discharge (OR 11.004, 95% CI 1.196–101.24, $p = 0.034$), impact of duration of hospitalization was supported (OR 1.034, 95% CI 1.007–1.062, $p = 0.014$) Moreover, the pregnancy number of the MMC neonate was significant in operations ≥ 48 h (OR 1.31, 95% CI 1.032–1.664, $p = 0.026$; Table 7). Neonates with larger head circumference (95% confidence interval [CI] 0.476–1.995, $p = 0.04$) and longer duration of hospitalization stay (95% confidence interval [CI] 0.358–1.867, $p < 0.001$; Table 2) had significantly higher rates of CNS infection. This trend is also positively supported by the multiple logistic regression analysis for both characteristics, respectively (OR 1.576, 95% CI 1.14–2.18, $p = 0.006$) and

Table 4 Prognostic factors for wound dehiscence/CSF discharge at MMC + shunt operations

	Operations (MMC + Shunt)		*p*	Effect Size [95%CI]
	Wound Dehiscence/CSF Discharge at MMC site			
	No	Yes		
	(*n* = 65)	(*n* = 6)		
Gender (Male), $_{n\ (\%)}$	31 (47.7)	0 (0)	**0.032**[f]	0.216[W] [0.103/0.330]
Length (cm), $_{median\ (min/max)}$	47 (38/55)	46.5 (43/48)	0.216[u]	
Head circumference (cm), $_{median\ (min/max)}$	36 (30/56)	35 (33/40.5)	0.456[u]	
Body weight (gr), $_{mean\ (SD.)}$	3115.63 (549.5)	2954 (343.84)	0.29[t]	
BMI (child), $_{mean\ (SD.)}$	23.27 (4.17)	23.39 (3.37)	0.942[t]	
Maternal age, $_{median\ (min/max)}$	28 (18/44)	28.5 (23/33)	0.919[u]	
In which pregnancy MMC, $_{median\ (min/max)}$	3 (1/11)	3 (1/4)	0.908[u]	
Postpartum MMC operation day, $_{median\ (min/max)}$	2 (0/15)	2.5 (0/11)	0.913[u]	
Chiari II malformation, $_{n\ (\%)}$	45 (69.2)	5 (83.3)	0.662[f]	
Postpartum shunt operation day, $_{median\ (min/max)}$	13 (1/74)	16 (11/27)	0.222[u]	
Orthopedic anomaly, $_{n\ (\%)}$	18 (27.7)	3 (50)	0.352[f]	
Rib anomaly, $_{n\ (\%)}$	9 (13.8)	3 (50)	0.056[f]	
Kyphosis, $_{n\ (\%)}$	11 (16.9)	2 (33.3)	0.301[f]	
Scoliosis, $_{n\ (\%)}$	8 (12.3)	3 (50)	**0.044**[f]	0.220[W] [0.095/0.345]
Neurologic status, $_{n\ (\%)}$			0.521[ff]	
Paraplegic	36 (55.4)	5 (83.3)		
Paraparetic	15 (23.1)	1 (16.7)		
Normal	14 (21.5)	0 (0)		
Newborn exitus (Ex), $_{n\ (\%)}$	1 (1.5)	1 (16.7)	-	
Duration of hospitalization (day), $_{median\ (min/max)}$	26 (10/109)	45 (31/158)	**0.009**[u]	1.162[d] [0.304/2.020]
Gestational age, $_{median\ (min/max)}$	38 (35/39)	38 (35/39)	0.999[u]	

[c]Pearson Chi-Square Test (Monte Carlo), [u]Mann Whitney U Test (Monte Carlo), [t]Independent Sample T Test (Bootstrap), [ff]Fisher Freeman Halton Test (Monte Carlo), [f]Fisher Exact Test (Monte Carlo), [W]Cramér's w Value, [d]Cohen's d Value, **CI**: Confidence interval, SD.: Standard deviation, min: Minimum, max: Maximum

(OR 1.034, 95% CI 1.007–1.06, $p = 0.011$; Table 7). These neonates with MMC were the outcome of a median 3.5 (2/4) pregnancy for their mothers (95% confidence interval [CI] 0.358–1.867, $p = 0.025$; Table 2). Multiple logistic regression analysis did not reveal any significant impact of number of pregnancy of the MMC neonate (OR 1.707, 95% CI 0.983–2.965, $p = 0.058$; Table 7).

A total of 26 (19.4%) neonates had kyphosis, with 9 (34.6%) undergoing kyphectomy in their later follow-up. All of them were paraplegic. Kyphectomy was performed in ≤ 48 h in 2 neonates and > 48 h in 7. The rationale of kyphectomy in neonates was to improve the functional outcome, to correct the MMC closure surgery-born skin closure defect, and to provide early restoration of kyphosis. Neonatal kyphectomy was performed on 6 females and 3 males. The mean time of surgery was 4 days. All neonates had S-shaped deformities in the lumbar vertebrae. In five neonates, correction was done by removing one vertebra, whereas a partial vertebrectomy was done in four. There were no severe complications, and wound closure was successful in all neonates except for one. The mean preoperative kyphosis of 75.6° (range, 50°- 90°) was improved to 35° (range, 15°–55°) by the end of follow-up.

Prognostic factors for kyphectomy in kyphotic neonates included MMC neonate pregnancy number (95% confidence interval [CI] 0.319–2.221, $p = 0.049$), postpartum MMC repair operation day (95% confidence interval [CI] 1.776–4.221, $p < 0.001$), number of previous operations (95% confidence interval [CI] 0.319–2.221, $p < 0.001$), presence and number of concurrent surgeries (95% confidence interval [CI] − 1.011–1.761, $p < 0.001$ and 95% confidence interval [CI] 0.168–1.255, $p < 0.001$, respectively), and history of Chiari II operation (95% confidence interval [CI] 0.291–0.857, $p = 0.002$; Table 6). Among these associations, multiple logistic regression analysis only supported the one with the postpartum MMC operation day (OR 1.655, 95% CI 1.011–2.708, $p = 0.045$; Table 7).

Table 5 Prognostic factors for wound dehiscence/CSF leak in early and late MMC repair operations

	Timing of MMC Repair Operation						
	≤ 48 Hours			> 48 Hour			
	Wound Dehiscence/CSF Leak at MMC site		*p*	Wound Dehiscence/CSF Leak at MMC site		*p*	Effect Size [95%CI]
	No ($n=54$)	Yes ($n=5$)		No ($n=69$)	Yes ($n=6$)		
Central Nervous System Infection, n (%)	2 (3.7)	0 (0)	0.999[f]	8 (11.6)	0 (0)	0.999[f]	
Gender (Male), n (%)	25 (46.3)	2 (40)	0.999[f]	38 (55.1)	1 (16.7)	0.099[f]	
Length (cm), mean (SD.)	47.52 (3)	47.4 (0.89)	0.841[t]	47.56 (3.07)	47.67 (4.03)	0.938[t]	
Head circumference (cm), median (min/max)	35 (30/56)	34 (33/36)	0.460[u]	35 (31/43)	34.75 (34/40.5)	0.988[u]	
Body weight (gr), mean (SD.)	3122.19 (574.99)	2976.8 (375.07)	0.402[t]	3034.7 (462.7)	3240 (699.71)	0.436[t]	
BMI (child), mean (SD.)	24.42 (4.56)	25.13 (2.73)	0.618[t]	24.29 (4)	26.02 (6.63)	0.521[t]	
Maternal age, median (min/max)	28.5 (17/43)	27 (21/36)	0.877[u]	27 (17/44)	30 (20/34)	0.799[u]	
In which pregnancy is MMC, median (min/max)	3 (1/11)	3 (2/4)	0.532[u]	2 (1/8)	1 (1/3)	0.246[u]	
Number of operations, median (min/max)	2 (1/4)	2 (1/2)	0.945[u]	2 (1/4)	2 (1/4)	0.099[u]	
Concurrent surgeries, n (%)			0.999[ff]			0.221[ff]	
MMC	18 (33.3)	2 (40)		30 (43.5)	1 (16.7)		
MMC + Shunt	34 (63)	3 (60)		31 (44.9)	3 (50)		
MMC + Kyphectomy	0 (0)	0 (0)		1 (1.4)	0 (0)		
MMC + Shunt + Kyphectomy	1 (1.9)	0 (0)		2 (2.9)	0 (0)		
MMC + Shunt + Chiari	0 (0)	0 (0)		2 (2.9)	1 (16.7)		
MMC + Shunt + Kyphectomy + Chiari	1 (1.9)	0 (0)		3 (4.3)	1 (16.7)		
Shunt operation, n (%)	36 (66.7)	3 (60)	0.999[f]	38 (55.1)	5 (83.3)	0.231[f]	
Kyphectomy, n (%)	2 (3.7)	0 (0)	0.999[f]	6 (8.7)	1 (16.7)	0.456[f]	
Chiari Operation, n (%)	1 (1.9)	0 (0)	0.999[f]	5 (7.2)	2 (33.3)	0.094[f]	
Hydrocephalus, n (%)	37 (68.5)	3 (60)	0.653[f]	43 (62.3)	5 (83.3)	0.410[f]	
Chiari II malformation, n (%)	30 (55.6)	2 (40)	0.652[f]	47 (68.1)	5 (83.3)	0.660[f]	
Postpartum shunt operation day, median (min/max)	6 (0/74)	12 (0/22)	0.708[u]	7 (0/43)	14 (0/38)	0.171[u]	
Orthopedic anomaly, n (%)	16 (29.6)	2 (40)	0.636[f]	20 (29)	3 (50)	0.363[f]	
Rib anomaly, n (%)	7 (13)	1 (20)	0.531[f]	6 (8.7)	3 (50)	**0.020[f]**	0.269[W] [0.144/0.395]
Kyphosis, n (%)	12 (22.2)	1 (20)	0.999[f]	11 (15.9)	2 (33.3)	0.277[f]	
Scoliosis, n (%)	8 (14.8)	2 (40)	0.196[f]	3 (4.3)	2 (33.3)	**0.048[f]**	0.217[W] [0.074/0.359]
Neurologic status, n (%)			0.585[ff]			0.409[ff]	

Table 5 (continued)

	Timing of MMC Repair Operation						
	≤ 48 Hours			> 48 Hour			
	Wound Dehiscence/CSF Leak at MMC site		*p*	Wound Dehiscence/CSF Leak at MMC site		*p*	Effect Size [95%CI]
	No ($n=54$)	Yes ($n=5$)		No ($n=69$)	Yes ($n=6$)		
Paraplegic	26 (48.1)	3 (60)		35 (50.7)	5 (83.3)		
Paraparetic	15 (27.8)	2 (40)		11 (15.9)	0 (0)		
Normal	13 (24.1)	0 (0)		23 (33.3)	1 (16.7)		
Newborn exitus (Exitus), n (%)	2 (3.7)	0 (0)	0.999[f]	1 (1.4)	1 (16.7)	0.155[f]	
Duration of hospitalization (day), median (min/max)	22 (2/103)	35 (11/62)	0.086[u]	22 (4/109)	45 (25/158)	**0.030[u]**	1.496[d] [0.628/2.364]
Gestational age, median (min/max)	38 (38/39)	38 (38/38)	0.594[u]	38 (35/39)	38 (35/39)	0.242[u]	

[f]Fisher Exact Test (Monte Carlo), [t]Independent Samples T Test (Bootstrap), [ff]Fisher Freeman Halton Test (Monte Carlo), [u]Mann Whitney U Test (Monte Carlo), [w]Cramér's w Value, [d]Cohen's d Value, **CI**: Confidence interval, SD.: Standard Deviation, min: Minimum, max: Maximum

Discussion

MMC is the most common form of closed spinal spina bifida in neonates. The higher risk of CNS infection in MMC is noteworthy because infected neonates may have permanent impairments, such as lower limb paralysis, bladder-bowel dysfunction, and sexual dysfunction [13]. In this study, we present a decade of tertiary center experience in the surgical management of 134 neonates with closed myelomeningocele (MMC).

NTDs can be caused by genetic and nongenetic origins. An increase in having another affected fetus after a previous neonate with MMC, in addition to the normal 0.2% risk, can be interpreted as proof of the genetic factor. Nonetheless, NTDs are rare in families with slightly sporadic distribution. The literature suggests that nongenetic factors have a significant impact [30]. Our results revealed no significant relationship between MMC characteristics and maternal age and the prevalence of MMC neonates.

Once the diagnosis is established, immediate surgery is recommended to repair the MMC sac within 24–48 h of birth to reduce the risk of infection [31, 32]. We performed MMC repair surgeries for 33.9% of neonates and MMC repair with shunt surgeries for 62.7% in ≤48 h. However, in the entire series, 55% of the neonates had postpartum MMC repair surgery at a median of 3 days, and 57.3% had a shunt surgery at a median of 7 days. We attributed the delay to the need for preoperative radiologic imaging and other technical problems. Consequently, the rate of wound dehiscence/CSF discharge at the MMC site in the >48 h operation group was 8%, slightly higher than the rates reported in the literature [33]. But the CNS infection rate was 10.7%, which was lower than the previously reported 18% rates [34].

MMC is a medical condition that is accompanied by several other spinal deformities and organ anomalies; therefore, in the absence of initial surgical repair, close follow-up in the intensive care unit, and recurrent hospitalizations, it may cause life-threatening complications. Hydrocephalus and Chiari type II malformation are the most prevalent concomitant anomalies in neonates with MMC (4). The top two anomalies in our series were hydrocephalus (65.7%) and Chiari type II malformation (62.7%), consistent with those in the literature. Other associated orthopedic anomalies (30.6%), kyphosis (19.4%), rib anomalies (12.7%), and scoliosis (11.2%), which we presented in our series, are consistent with the literature [4, 22, 35].

Following MMC repair, surgical management of neonates with concomitant deformities and conditions ranges from observation to complex joint operations. In the literature, many studies reported the need for shunting surgery of MMC-related hydrocephalus in the first place following MMC closure, pointing out a VPS rate between 57–86%

Table 6 Prognostic factors for kyphectomy in kyphotic neonates with MMC

Kyphosis (Yes)	Kyphectomy		*p*	Effect Size [95%CI]
	No	Yes		
	(*n* = 17)	(*n* = 9)		
Wound Dehiscence/CSF Discharge at MMC site$_{n\,(\%)}$	2 (11.8)	1 (11.1)	0.999[f]	
Central Nervous System Infection, $_{n\,(\%)}$	2 (11.8)	1 (11.1)	0.999[f]	
Gender(Male), $_{n\,(\%)}$	10 (58.8)	3 (33.3)	0.411[f]	
Length (cm), $_{median\,(min/max)}$	45 (41/50)	47 (44/49)	0.529[u]	
Head circumference (cm), $_{median\,(min/max)}$	35 (30/43)	35.5 (33/43.5)	0.625[u]	
Weight (gr), $_{median\,(min/max)}$	2830 (2000/3688)	2780 (1950/3800)	0.784[u]	
BMI (child), $_{median\,(min/max)}$	22.22 (17.5/29.8)	20.76 (15.92/34.89)	0.565[u]	
Maternal age, $_{median\,(min/max)}$	26 (20/38)	28 (18/40)	0.638[u]	
Kyphosis angle (preop/postop), median (min/max)	**-/-**	**80 (50/90)/45 (15/65)**	**0.004**[y]	**5.695**[d] **[2.820/8.570]**
In which pregnancy is MMC, $_{median\,(min/max)}$	3 (1/11)	2 (1/7)	0.217[u]	
Postpartum MMC operation day (day), $_{median\,(min/max)}$	2 (0/6)	4 (1/12)	**0.049**[u]	1.270[d] [0.319/2.221]
Number of operations, $_{median\,(min/max)}$	2 (1/2)	4 (2/4)	**< 0.001**[u]	2.999[d] [1.776/4.221]
Concurrent surgeries, $_{n\,(\%)}$			**< 0.001**[ff]	
MMC	4 (23.5)	0 (0)	P(A—C) = **< 0.001**	0.375[W] [− 1.011/1.761]
MMC + Shunt	13 (76.5)	0 (0)	P(B—C) = **< 0.001**	0.462[W] [− 0.307/1.230]
MMC + Kyphectomy	0 (0)	1 (11.1)[A B]	P(A—D) = **< 0.001**	0.625[W] [− 0.355/1.605]
MMC + Shunt + Kyphectomy	0 (0)	3 (33.3)[A B]	P(B—D) = **< 0.001**	0.712[W] [0.168/1.255]
MMC + Shunt + Chiari	0 (0)	0 (0)		
MMC + Shunt + Kyphectomy + Chiari	0 (0)	5 (55.6)		
Shunt operation, $_{n\,(\%)}$	13 (76.5)	8 (88.9)	0.628[f]	
Chiari operation, n (%)	0 (0)	5 (55.6)	**0.002**[f]	0.574[W] [0.291/0.857]
Hydrocephalus, $_{n\,(\%)}$	14 (82.4)	9 (100)	0.529[f]	
Chiari II malformation, $_{n\,(\%)}$	10 (58.8)	7 (77.8)	0.418[f]	
Postpartum shunt operation day, $_{median\,(min/max)}$	12 (0/74)	12 (0/38)	0.603[u]	
Orthopecid anomaly, $_{n\,(\%)}$	8 (47.1)	5 (55.6)	0.999[f]	
Rib anomaly, $_{n\,(\%)}$	4 (23.5)	4 (44.4)	0.382[f]	
Scoliosis, $_{n\,(\%)}$	7 (41.2)	1 (11.1)	0.190[f]	
Neurologic status (paraparetic), $_{n\,(\%)}$	2 (11.8)	0 (0)	0.529[f]	
Newborn Exitus (Ex), $_{n\,(\%)}$	1 (5.9)	1 (11.1)	0.999[f]	
Duration of Hospitalization (Day), $_{median\,(min/max)}$	32 (7/158)	24 (9/68)	0.905[u]	
Timing of MMC repair operation (> 48 h), $_{n\,(\%)}$	6 (35.3)	7 (77.8)	0.097[f]	
Gestational age, $_{median\,(min/max)}$	38 (38/39)	38 (35/39)	0.466[u]	

[f]Fisher Exact Test (Monte Carlo), [u]Mann Whitney U Test (Monte Carlo), [ff]Fisher Freeman Halton Test, [y]Wilcoxon Signed Ranks Test(Monte Carlo), [W]Cramér's w Value, [d]Cohen's d Value, **CI**: Confidence interval, [A]Statistically significant in comparison to MMC group, [B]Statistically significant in comparison to MMC + Shunt group, Min: Minimum, max: Maximum, MMC: Meningomyelocele

[31, 36–41]. Corresponding to this data, almost half of our neonates have been operated on at least twice in ≤ 48 h, with 63% undergoing concurrent MMC repair and shunt surgeries. One neonate had MMC, hydrocephalus, and kyphosis surgery simultaneously, whereas another had MMC, hydrocephalus, kyphosis, and Chiari II surgery performed. MMC closure and kyphectomy were performed on this patient in the first step. VP Shunt operation was the second step. The final step was performing the Chiari II operation on the neonates with clinically positive Chiari II-related symptoms.

Only two neonates in the ≤ 48 h underwent complex surgeries. One underwent MMC repair, shunt operation with kyphectomy, and another underwent MMC repair, shunt operation, kyphectomy, and Chiari II operation. None experienced wound dehiscence/CSF discharge at the MMC site or CNSI (Table 5). On the other hand, more neonates operated on > 48 h underwent complex surgeries. MMC repair and shunt surgery were performed in 45% of cases. One neonate underwent MMC repair and kyphectomy. For more complex surgeries besides MMC repair and shunt surgery, two underwent kyphectomy, and two underwent Chiari type II correction. In this group, three neonates underwent MMC, hydrocephalus, kyphosis, and Chiari II surgery. Wound dehiscence occurred in one neonate, each with three and four complex surgeries. The only neonate with a total of four complex surgeries in the > 48 h group developed

Table 7 Gestational age-adjusted logistic regression analyses results for dependent variables and reference groups

Adjusted for Gestational age		B (SE.)	*P* value	Odds Ratio (95% C.I.)
Dependent Variable: Timing of MMC Repair Operation				
Reference Groups: > 48 h	**In which pregnancy is MMC (↓)**	0.27 (0.12)	**0.026**	1.31 [1.032—1.664]
	Scoliosis	1.59 (0.69)	**0.02**	4.921 [1.281—18.911]
	Duration of hospitalization (Day) (↑)	0.02 (0.01)	0.071	1.019 [0.998—1.039]
	Accuracy Ratio	**≤ 48 h: 45.6**	**> 48 h: 76.1**	**Total: 62.5—Cut off Point: 0.53**
Timing of MMC Repair Operation (> 48 h)				
Dependent Variable: Central Nervous System Infection	**Head circumference (cm) (↑)**	0.46 (0.17)	**0.006**	1.576 [1.14—2.18]
Reference Groups: Yes	**In which pregnancy is MMC (↑)**	0.53 (0.28)	0.058	1.707 [0.983—2.965]
	Duration of hospitalization (Day) (↑)	0.03 (0.01)	**0.011**	1.034 [1.007—1.06]
	Accuracy Ratio	**No: 82.5**	**Yes: 75.0**	**Total: 81.7—Cut off Point: 0.15**
Dependent Variable: Wound Dehiscence/CSF Discharge at MMC site				
Reference Groups: Yes	**Scoliosis**	1.61 (0.74)	**0.031**	4.999 [1.163—21.481]
	Duration of hospitalization (Day) (↑)	0.03 (0.01)	**0.009**	1.028 [1.007—1.049]
	Accuracy Ratio	**No: 99.2**	**Yes: 18.2**	**Total: 92.5—Cut off Point: 0.44**
Dependent Variable: Central Nervous System Infection				
Reference Groups: Yes	**Head circumference (cm) (↑)**	0.14 (0.07)	0.054	1.154 [0.998—1.334]
	Duration of hospitalization (Day) (↑)	0.02 (0.01)	**0.027**	1.024 [1.003—1.045]
	Accuracy Ratio	**No: 98.4**	**Yes: 0.0**	**Total: 91.0—Cut off Point: 0.42**
Operations (MMC + Shunt)				
Dependent Variable: Wound Dehiscence/CSF Discharge at MMC site	**Scoliosis**	2.17 (0.99)	**0.029**	8.728 [1.251—60.892]
Reference Groups: Yes	**Duration of hospitalization (Day) (↑)**	0.03 (0.01)	**0.024**	1.03 [1.004—1.056]
	Accuracy Ratio	**No: 98.5**	**Yes: 16.7**	**Total: 91.5—Cut off Point: 0.50**
Timing of MMC Repair Operation (> 48 h)				
Dependent Variable: Wound Dehiscence/CSF Discharge at MMC site	**Scoliosis**	2.4 (1.13)	**0.034**	11.004 [1.196—101.24]
Reference Groups: Yes	**Duration of hospitalization (Day) (↑)**	0.03 (0.01)	**0.014**	1.034 [1.007—1.062]
	Accuracy Ratio	**No: 100.0**	**Yes: 33.0**	**Total: 94.7—Cut off Point: 0.50**
Kyphosis (Yes)				
Dependent Variable: Kyphectomy	**Postpartum MMC operation day (day) (↑)**	0.5 (0.25)	**0.045**	1.655 [1.011—2.708]
Reference Groups: Yes	**Accuracy Ratio**	**No: 64.7**	**Yes: 85.7**	**Total: 70.8—Cut off Point: 0.25**

Multiple Logistic Regression (Method = Backward Stepwise (Wald)), C.I.: Confidence interval B: regression coefficients *SE* Standard Error

a CNS infection and died. Even though delayed surgery is more prone to local disturbances (wound dehiscence/CSF discharge), effective surgical correction of accompanying anomalies and deformities, and antibiotic treatment with close follow-up of symptoms effectively control systemic infection, which follows literature [42].

Kyphosis is one of the most common spinal deformities in neonates with MMC. Severe kyphosis may pose a more significant threat than the form or size of the MMC lesion for repair surgery [43]. It is the most severe deformity, affecting around 15% of neonates [44, 45]. Our series comprised 19.4% kyphotic neonates, which is slightly higher than the rate reported in the literature. Indications for kyphectomy included prevention of poor prognosis due to increasing kyphotic angle, improvement of pain, and providing functionality. Most (77%) of the kyphectomy surgery was performed in the delayed group. Although neonatal kyphectomy is considered a safe procedure, one of the two kyphectomied neonates was lost to wound dehiscence and subsequent CNSI, as previously mentioned. The long-term outcome of kyphectomy was delayed instability in neonates [27].

In our study, the postpartum MMC operation day, the presence and number of concurrent surgeries, and the Chiari II operation were significant prognostic factors for kyphectomy. The multiple logistic regression analysis supported the postpartum MMC operation day as a significant prognostic factor. Based on our results, we advocate that the MMC repair operation and kyphectomy be performed concurrently because this approach results in shorter operation times, less blood loss, longer temporary hospital stays, and better deformity repair.

Surely this study has some limitations. The retrospective study design introduces intrinsic bias, such as incomplete data and follow-up, despite the utmost care provided. Moreover, this study employed a Monte Carlo simulation, which may introduce certain limitations due to the small sample size. A key assumption of the simulation is that the sample accurately represents the population; however, this may not hold true for all variables. As a result, this limitation may increase variability in the results and reduce their generalizability. Therefore, the findings should be interpreted with caution and validated in larger samples.

Conclusion

The results of our study showed that the primary predictor of prognosis for the neonates with MMC and accompanying severe congenital anomalies is not the timing of MMC sac repair (early surgery vs. delayed surgery) but the successful surgical and medical management of accompanying deformities and conditions, such as kyphosis, hydrocephalus and Chiari type II. Our gestational age-adjusted multiple regression analysis did not support a trend to the superiority of early surgical intervention ($\leq$ 48 h) against CNSI and wound dehiscence/CSF discharge. The radiologic presence of the Chiari II malformation is not an adequate indication for surgical correction. The severity of the symptoms related to these circumstances in the neonate is critical for decision-making regarding the timing and technique of the corrective surgeries in these patients.

Author contributions Conceptualization was done by Çağlar Türk, Mahmut Çamlar, and Nail Özdemir. Data curation was carried out by Çağlar Türk, Umut Tan Sevgi and Ozan Akgül. Formal analysis was handled by Senem Alkan Özdemir. Methodology was developed by Çağlar Türk, Mahmut Çamlar, and Nail Özdemir. Software contributions were made by Senem Alkan Özdemir. The original draft was written by Çağlar Türk, while Nail Özdemir and Füsun Özer contributed to the review and editing.

Data availability No datasets were generated or analysed during the current study.

Declarations

This study received no funding or financial support during the preparation of this manuscript. Clinical trial number: not applicable. The study protocol was approved by the Ethics Committee of the University of Health Sciences, Izmir Tepecik Training and Research Hospital (Protocol Number: 2022/12–11). This retrospective study was conducted in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The requirement for informed consent for study participation was waived by the ethics committee due to the study's retrospective nature.

Competing interest The authors declare no competing interests.

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