

# Review on myelomeningocele management and its current status in Saudi Arabia

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## ABSTRACT

يوجد تغييرات كبيرة وجديدة في مجال معالجة القيلة النخاعية السحائية، وفي هذه المراجعة نركز على أهم مستحدثات الطرق في مجال معالجة القيلة النخاعية السحائية وأوضاعها الحالية بالمملكة العربية السعودية. عبء القيلة النخاعية السحائية: مدى الانتشار في المملكة العربية السعودية يتراوح بين 0.44-1.46/1000 مولود. 9.7% فقط من النساء السعوديات الحوامل يستخدمن حمض الفوليك قبل الحمل. وتقدر التكلفة «تقريباً» لكل مريض 1,417,500 ريال. يجب أن يؤخذ قرار الإجهاض بحذر في البلدان الإسلامية، والجانب الآخر هو إصلاح القيلة النخاعية السحائية عن طريق الجراحة داخل الرحم، والتي أظهرت نتائج أفضل للأعصاب الحركية ولكن بنسبة خطوره أعلى على صحة الحمل، ومع ذلك فقد زاد هذا الإجراء من فرص نجاح إجراء تصريف عبر البطن الثالث بالمنظار وتقليل الحاجة إلى التحويلة البطنيّة الصفاقية. ومع مرور سبع سنوات على التوجه العالمي نحو جراحة الجنين داخل الرحم لازالت الحاجة لبعض الخطوات القليلة اللازمة لإنشاء هذه الخدمة في المملكة العربية السعودية. تتطلب رعاية متعددة التخصصات لمرضى القيلة النخاعية السحائية. ينبغي أن يتم الإغلاق الجراحي في غضون 72 ساعة بعد الولادة للحد من خطر العدوى بغض النظر عن النقاش في وقت عمل التحويلة. إن التقدم في رعاية مرضى القيلة السحائية أصبح يسمح للمرضى بالبقاء على قيد الحياة حتى سن البلوغ، ومع ذلك فيجب اتخاذ إجراءات لتحسين نوعية الرعاية في معالجة القيلة النخاعية السحائية في المملكة العربية السعودية.

Major approaches have emerged in the field of myelomeningocele (MMC) management. The prevalence of MMC in Kingdom of Saudi Arabia is 0.44-1.46/1000 births. Nine point seven percent of pregnant Saudi women take folic acid before conception; MMC is estimated to result in 1,417,500 Saudi Riyals (SAR) in lifetime costs per patient. Abortion should be performed cautiously in Muslim countries; another option may be the intrauterine foetal surgical repair of MMC, which has better neuromotor outcomes and reduces the need for ventriculoperitoneal shunt, albeit with a higher risk of obstetric complications. Seven years after intrauterine foetal surgery emerged, there is a need to establish this service in Kingdom of Saudi Arabia. A multidisciplinary approach is required for MMC

patients; surgical closure should be carried out within 72 hours after birth to reduce the risk of infection. Advancing MMC care allows patients to survive to adulthood, and action must be taken to improve the quality of MMC care in Kingdom of Saudi Arabia.

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Neural tube defects represent one of the major disabling and challenging pathologies for healthcare providers; they require skilled multidisciplinary diagnostic and management approaches. For many decades, myelomeningocele (MMC) management remained static, with no major advancements being made in the field; as a result, the associated morbidity and mortality continued to be high. However, in the last decade, major developments in and new management strategies for MMC management have emerged, and some have been ground-breaking. In this review, we highlight the major updates on MMC management and its current status in Kingdom of Saudi Arabia.

***Myelomeningocele burden.*** Neural tube defects represent one of the most disabling and challenging pathologies for healthcare providers across multiple

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disciplines. These defects emerge as early as the antenatal period, when obtaining an accurate diagnosis requires skill and experience; in the postnatal period, MMC closure is required, and the use of a ventriculoperitoneal (VP) shunt is associated with potential complications. Epilepsy and low intelligence quotient (IQ) are potential major neurological complications of MMC.<sup>1,2</sup> Moreover, neural tube defects necessitate rehabilitation and multiple subspecialty clinic visits, as well as potential surgeries for bowel, bladder, and leg deformities. This pathology results from a failure of the neural tube to close, which leads to spinal cord exposure, known as spina bifida (SB), of which MMC is the most common type. Despite the use of measures that have been established to reduce the prevalence of SB in Kingdom of Saudi Arabia, which include health education, antenatal supplementation of folic acid, and flour fortification, the prevalence of MMC in Kingdom of Saudi Arabia remains the same.<sup>3</sup> Multiple studies conducted in Kingdom of Saudi Arabia have quantified the prevalence of MMC from 1979-2005, which ranged from 0.8-1.46/1000 births. However, after implementing the food fortification policy that was adopted by the Saudi government in the year 2000, the prevalence of MMC ranged from 0.44-1.46/1000 births (Table 1).<sup>4</sup> Saudi health authorities adopted folic acid supplementation, one of the most effective preventives for MMC, for pregnant women decades ago, taking into consideration the appropriate dose and timing of folic acid before conception or even initiating folic acid supplementation among all married women to reduce the burden of unplanned pregnancy.<sup>5</sup> However, only 9.7% of pregnant Saudi women used folic acid supplementation before conception with continuation throughout pregnancy, which is far below the expectation for such an ambitious plan.<sup>6</sup> Other studies have reported that approximately 4% of Saudi women use folic acid during pregnancy, 8.3% of whom have had previous children with congenital anomalies.<sup>4,7</sup> Saudi females appear to possess risk factors for SB development in their offspring, resembling the risk factors published

internationally that were associated with higher rates of consanguinity.<sup>8</sup> In 2015, it was estimated that 13% of SB cases worldwide could have been prevented with the supplementation of folic acid.<sup>9</sup> The burden associated with SB is higher in low- and middle-income countries than in high-income countries.<sup>10</sup> The prevention of neural tube defects could be improved if low-income countries adopted food fortification practices in their communities.<sup>11</sup> In 2010, it was found that children with SB and their caregivers suffered from the huge burden of the disease physically, mentally, emotionally, and economically, with an average lifetime direct medical cost per person of 285,959-378,000 American dollars (USD).<sup>12</sup> The lifetime direct medical cost for patients with MMC is significant, with most costs associated with inpatient care; these costs are related to treatment at the initial diagnosis in childhood, and for comorbidities in adult life. The lifetime indirect costs for patients with MMC are even greater due to increased morbidity and premature mortality.

Caregiver time costs are also significant. There are no precise numbers on the care-related costs faced by MMC patients in Kingdom of Saudi Arabia; however, it can be presumed that since the birth rate in Kingdom of Saudi Arabia is estimated to be 18.7/1000 population, this can translate into  $18.7/1,000 \times 30,000,000$  (Saudi population) = 561,000 total new births/year. As such, there are approximately 785 new MMC patients/year. Based on the 2003 costs associated with MMC in Kingdom of Saudi Arabia, it can be calculated that there are  $378,000 \text{ USD} \times 3.75 = 1,417,500 \text{ SAR}$  lifetime costs per patient; if the estimated number of affected children is 785 per year, then more than one billion SAR are added to the expected annual cost. There were cost savings of 607 million USD/year associated with those SB cases that were prevented using folic acid fortification in the United States of America.<sup>13</sup>

**Perinatal care.** The diagnostic approach in the prenatal phase starts with sonographic screening to detect congenital anomalies, including SB; however, magnetic resonance imaging is the diagnostic imaging

**Table 1 -** List of MMC incidence and prevalence studies in different provinces in the Kingdom of Saudi Arabia.

Study	Year	Province	Incidence (per 1000 live births)	Prevalence (per 1000 live births)
Magbool et al, <sup>4</sup>	1989	Eastern province	1.83	--
El-Awad et al, <sup>5</sup>	1992	Southern province	0.82	--
Asindi et al, <sup>6</sup>	2001		0.78	--
Safdar et al, <sup>7</sup>	2007	Western province	0.76	--
Seidahmed et al, <sup>9</sup>	2014	Central province	--	1.2

MMC - myelomeningocele

tool that allows early diagnosis during the first trimester.<sup>14</sup>

Any treatment or management options undertaken during this period must be carried out with much caution, especially in our conservative Muslim culture. We looked at this issue from 2 perspectives, as based on the opinion of the Islamic Fiqh (Jurisprudence) council, under the umbrella of the Muslim world league.<sup>15</sup> This council concluded that abortion can be accepted in cases when a foetus is expected to be disabled, as long as the foetus was conceived less than 4 months prior to the procedure, as based on the authentic narrations of the Prophet Mohammed, peace be upon him.<sup>15</sup> However, the major Islamic concerns regarding abortion are based on the following: the anticipated harm to the mother from continuing the pregnancy; the status of the foetus in terms of ensoulment before or after 4 months' gestation; and anomalies not compatible with life. The Islamic Fiqh council concluded that after 4 months, abortion is prohibited, except in the case when continuing with the pregnancy would pose a major risk for the mother's life (See the 12th Islamic Fiqh council meeting decisions, Makkah, Kingdom of Saudi Arabia, dated February 7, 1991, which corresponds to Rajab 7, 1410 Hijri calendar). There have been numerous debates exploring the possibility of performing an abortion after 4 months' gestation for patients with severe malformation and disabilities, reducing the burden on families and the healthcare system psychologically, mentally, emotionally, and economically.<sup>16</sup> We think that, as neurosurgeons and obstetricians, we must work on this fatwa (a ruling on a point of Islamic law given by a recognized authority) or opinion, giving parents the option to terminate a pregnancy if they elect to do so. This decision must go through official channels comprising religious and administrative authorities to render this a legal action and to standardize such action without abuse.

Another aspect of the care provided to MMC patients is antenatal surgery. In 2010, Adzick et al,<sup>17</sup> found that the intrauterine foetal surgical repair of MMC patients before the 26th week of pregnancy was associated with better motor outcomes and reduced shunt dependency, and this was related to reversed hindbrain herniation. However, the Management of Myelomeningocele Study (MOMS) trial revealed that there was a higher risk for spontaneous membrane rupture and preterm delivery at 34.1 weeks of gestation on average.

From a technical point of view, foetal surgery for MMC repair is similar to postnatal closure, although there are some technical variations. The Children's Hospital of Philadelphia (CHOP) has clinical experience in foetal intrauterine MMC repair, and their approach

has shown promising results in terms of hindbrain herniation reversal and a reduction in the need for a VP shunt; this is also associated with improved neuromotor and cognitive outcomes.<sup>18</sup>

Physicians who prefer open maternal-foetal surgery believe its risk is acceptable. However, its associated outcomes in terms of membrane complications, the age of gestation, and postoperative hospital length of stay were suboptimal.<sup>19</sup> To perform this procedure, consent from the mother in conjunction with a consultation to discuss the possible complications and benefits related to this management option should be obtained.<sup>20</sup> Intrauterine surgery was found to reduce the negative impact on families caring for children with SB; however, the uncertainty and unavailability of long-term outcomes make it difficult to predict the prognosis.<sup>21</sup> Also, post-trial complications differ from the trial results, which is questionable and requires additional studies.<sup>22</sup> Historically, and based on recent evidence, endoscopic third ventriculostomy (ETV) remained a controversial treatment option for this group of patients; however, ETV showed great and promising outcomes in children who underwent foetal surgery repair for MMC, reducing the need for VP shunt by 34.5% compared to 40% in the MOMS trial.<sup>23,24</sup>

Pre-tethering neural signals were found to be reproducible at the level below the lesion in intraoperative neurophysiological monitoring for foetal MMC repair, which is contrary to what was found for postnatal repair.<sup>25</sup> Conversely, considerable obstetric complications can occur, such as ruptured membranes, preterm delivery, and non-intact hysterotomy at delivery.<sup>26</sup> Specialists from Foetal therapy centres in Thailand, Hong Kong, India, and Singapore met to establish prenatal surgery guidelines in Asia with the aim of reducing the burden of the high prevalence of MMC in Asia.<sup>27</sup> Given that the incidence of MMC in kingdom of Saudi Arabia has not demonstrated major declines over the last few decades, that the legislation of elected abortion may or may not occur in the near future, and that kingdom of Saudi Arabia is one of the healthcare leaders in the region, it is expected that this type of service will begin to grow and expand; however, 7 years since the aforementioned evidence was published, this health service has not been established.

Larger centres in Kingdom of Saudi Arabia are expected to launch this service as soon as possible. Around the world, the future of foetal neurosurgery is promising for MMC and other pathologies, which can be treated prenatally with better outcomes.<sup>28</sup> In these situations, special ethical care must be considered.<sup>29</sup>

**Postnatal care.** Postnatal diagnosis relies on clinical presentation of a midline defect and magnetic resonance

imaging (MRI) findings of a cerebrospinal fluid (CSF)-filled sac with a neural placode (myelocele), which could be covered with meninges (myelomeningocele); this defect could be covered with skin (closed SB) or not (open SB).<sup>14</sup>

After MMC patients are born, they go through multiple surgeries and must be looked after by specialized teams. Their list of concerns is rather long, ranging from neurological deficits to sphincter disturbances, potential renal involvement, orthopaedic deformities, the need for rehabilitation, and so on.

From a neurosurgical perspective, the surgical closure of a spinal lesion should be carried out within 72 hours after birth to reduce the risk of central nervous system infection and to improve outcomes.<sup>30</sup> However, there is still much debate among neurosurgeons related to the timing of VP shunt insertion, whether at the same time as or performed in a separate procedure after the MMC is repaired. In the decades since Epstein,<sup>31</sup> published his paper in 1985 that advocated for simultaneous MMC repair and VP shunting, many papers have been published. Most of these papers are retrospective studies, and they have featured small numbers of patients.<sup>31-33</sup> Following their publication, debates have emerged related to the increased failure rates and VP shunt infections that occur after the simultaneous procedure; conversely, some neurosurgeons advocate for simultaneous procedures, even though there have been higher rates of cerebrospinal fluid leakage in babies who underwent MMC repair while awaiting VP shunt insertion.

The 2 largest studies conducted on this matter (the former of which was prospective collected data 189 cases, and the latter of which was retrospective collected data 127 cases).<sup>34,35</sup> Neither studies found any evidence to support the notion that the simultaneous procedure for MMC repair and VP shunt insertion increases the risk of shunt infection or malfunction. Therefore, neurosurgeons who advocate for the simultaneous procedure may decrease the associated risks by exposing the baby to anesthesia once, rather than twice.

Despite the findings of the ETV score study, and the estimated low success rate of ETV among babies with MMC, growing evidence from new studies is laying the foundation for the use of ETV with choroid plexus coagulation, which is emerging as a novel option for MMC management.<sup>36</sup> This approach appears to offer better treatment for hydrocephalus among infants with SB when compared with shunt placement.<sup>37</sup> Many factors have led to this management strategy, including shunt failures, shunt-related infections, and the associated consequences related to medical, economic,

and patient-related outcomes. Furthermore, shunts can be rather expensive in countries with limited medical resources, which also tend to have high prevalence and incidence of MMC (such as some African countries).<sup>38-41</sup>

For stable patients with mild to moderate hydrocephalus, observation with frequent head circumference and neuro-radiological follow-up is advised to reduce the rate of shunt placement.<sup>42,43</sup> Clinical assessment to determine the level of independence among MMC patients and their caregivers should also be performed, as should screening for social and emotional adjustment. Furthermore, special programs to train and facilitate these individuals' abilities to reach their maximum level of independence are required.<sup>44</sup>

The implementation of a care coordination system in SB clinics showed a reduced level of burden among families and patients.<sup>45</sup> Spina bifida requires a multidisciplinary approach from a variety of specialties, including paediatric neurosurgery, orthopaedics, neurology, urology, and rehabilitation, and the involvement of physiotherapists, occupational therapists, nutritionists, and social workers.<sup>46,47</sup> Unfortunately, the majority of MMC patients fail to receive adequate multidisciplinary care, despite the availability of these specialty care clinics due to a lack of SB care clinics.<sup>48</sup>

One model for SB services was proposed in 2000, integrating the medical and functional dimensions of patient perspectives.<sup>49</sup> This model is based on the basic concepts built on the disability coding (ICIDH-2) framework, which is able to identify the various medical, functional, and rehabilitative aspects of patients across their lifespans. The 3 main dimensions of ensuring comprehensive, coordinated, and long-term patient care include ensuring a patient's health, functional abilities, and active participation in his or her healthcare.

In conclusion, for SB patients to survive to adulthood, they require advanced facilitated care to help them across numerous developmental transitions.<sup>50</sup> To perform such intricate care, there is a need for multiple clinics and follow-ups. As such, some centres around the world have established SB clinics. These clinics aim to save time and resources for patients and healthcare systems alike while preventing complications before they appear.

To date, 4 centres have established SB services across Kingdom of Saudi Arabia; 2 of these services were established in the last 2 years. As the prevalence of SB and MMC are still relatively high, and given that the costs associated with complications and care are high, the SB clinic programme has great potential to improve MMC patients' quality of life while directly saving



healthcare resources and indirectly saving the resources of family caregivers and patients. New perspectives on the role of regenerative medicine in treating MMC, especially with early detection during intrauterine life, are necessary.<sup>51</sup>

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