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ORIGINAL ARTICLE

Neurogenic Bladder in Patients with Mylomeningocele in Pediatric Age

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ABSTRACT

Myelomeningocele (MMC) is congenital nervous system malformation caused by neurulation process failure during pregnancy. The prevalence varies by the continent, region, race, ethnicity and the time when assessed and patients present abnormalities of different organs. One of the most severe complications is renal failure.

Aim: Clinical evaluation of patients with MMC in Iraq and answering the question whether our treatment methods lead to renal function preservation.

Material and methods: Medical records of 28 patients in the period 2014.2019were evaluated retrospectively. The data included: age, sex, BMI Z-score WHO, place of residence, perinatal history, social situation, physical activity, urodynamic diagnosis, renal function, hydrocephalus diagnosis, and functioning of shunting procedures.

Results: They were no statistically significant differences in most studied parameters between boys and girls.

Keywords: Meningomyelocele, Epidemiological study, Neurogenic bladder, Renal function

INTRODUCTION

Definition Of Neurogenic Bladder: Neurogenic detrusor sphincter dysfunction (NDSD) can develop as a result of a lesion at any level in the nervous system, including the cerebral cortex, spinal cord or the peripheral nervous system.

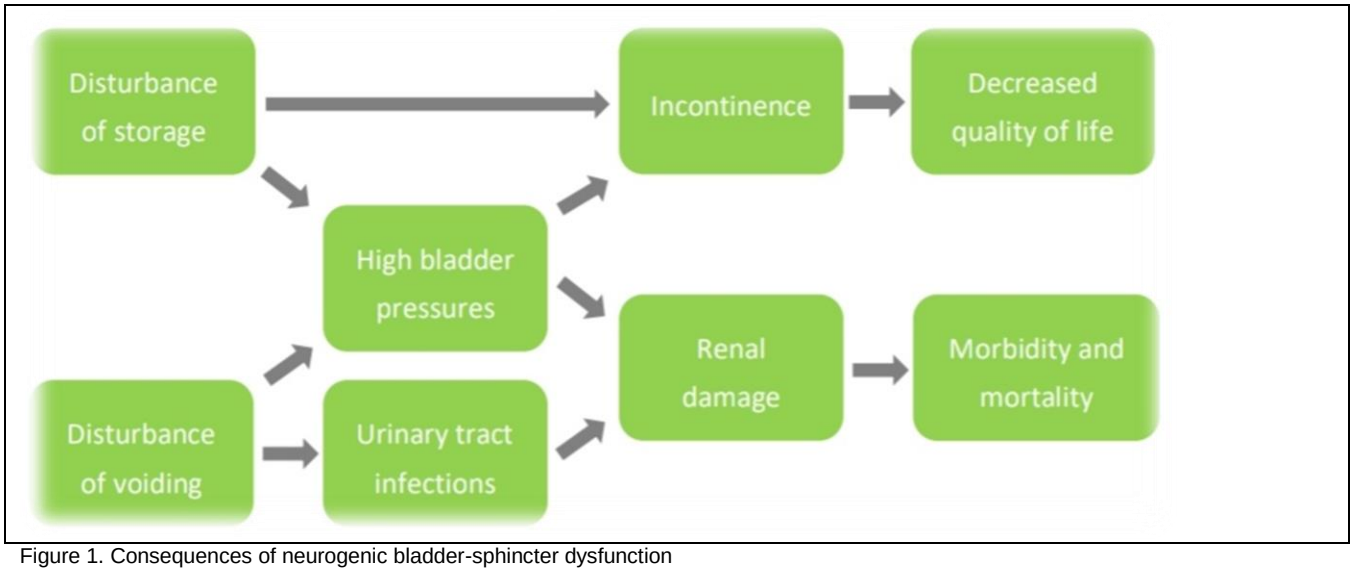


Figure 1. Consequences of neurogenic bladder-sphincter dysfunction

Classification Of Neurogenic Bladder

Table 1. Simplified classification of spinal dysraphism. Adapted from Tortori 2000.

Spinal dysraphism = neural tube defects
Open spinal dysraphism = Spina bifida cystica
Myelomeningocele MMC
Myelocele
Closed spinal dysraphism = Spina bifida occulta
With subcutaneous mass
Lipoma with dural defect (e.g. Lipo-MMC)
Without subcutaneous mass
□ Intradural lipoma
□ Filum terminale lipoma
□ Diastematomyelia
□ Dermal sinus
□ Caudal regression syndrome

Pathophysiology

Four major types are usually used to describe the detrusor-sphincter dysfunction:

1. Detrusor overactivity with sphincter overactivity (dyssynergia),
2. Detrusor overactivity with normal or underactive sphincter,
3. Detrusor underactivity with sphincter overactivity
4. Detrusor underactivity with sphincter underactivity (1,2,3)

Prenatal Screening and Newborn Care: Prenatal screening can identify many affected fetuses. Between the 16th and 18th weeks of pregnancy, maternal serum is analyzed routinely for alpha-fetoprotein (AFP), which is elevated when the fetus has an open myelomeningocele. If the AFP value is abnormal, highresolution ultrasonography

is used to detect specific abnormalities of the fetal head and back. If myelomeningocele still is suspected, amniocentesis is performed to analyze amniotic fluid concentrations of AFP and acetylcholinesterase, an enzyme found in cerebrospinal fluid. At the same time, chromosomes are evaluated to rule out conditions associated with myelomeningocele, such as trisomy 13. Typically, the lesion on the back is closed surgically within 72 hours (4,5,6)

Table 2. Functional Levels in Children Born With Myelomeningocele.

Level	Implications for mobility
High lumbarthoracic	Can walk for short distances using long leg (high) braces. By early adolescence, most use wheelchair for mobility.
Low lumbar	Can walk with short leg braces and forearm crutches.
High sacral	Can walk with a gluteal lurch using braces to stabilize the ankle and foot. Walking ability usually is retained through adolescence

Delivery of Care: Children born with myelomeningocele typically receive care from multiple clinicians, including orthopedists, orthotists, urologists, and neurosurgeons, as well as physical, occupational, and sometimes speech therapists (7,8,9).

Neurourologic Evaluation of Neurogenic Bladder/Urodynamics

This document included 5 specific standards or recommendations
surrounding the use of urodynamics in patients with NGB:

- C linicians should perform PVR(Post-void residual) assessment, either as part of a complete urodynamic assessment or separately, during initial urologic evaluation of patients with relevant neurologic conditions and as part of ongoing follow-up where appropriate. (Standard;
Strength of Evidence Grade B.)
- C linicians should perform a CMG during initial urologic evaluation of patients with relevant neurologic conditions with or without symptoms and as part of ongoing follow-up when appropriate. In patients with other neurologic diseases, physicians may consider CMG an option in the urologic evaluation in patients with lower urinary tract symptoms. (Recommendation; Strength of Evidence Grade C.)(10).
- C linicians should perform pressure flow analysis (PFS) during initial urologic evaluation of patients with relevant neurologic conditions with or without symptoms and as part of ongoing follow-up when appropriate, in patients with other neurologic disease and elevated PVR, or in patients with persistent symptoms. (Recommendation; Strength of Evidence Grade C.)
- When available, clinicians may perform fluoroscopy at the time of urodynamics (videourodynamics) in patients with relevant neurologic disease at risk for NGB, in patients with other neurologic disease and elevated PVR, and in patients with urinary symptoms. (Recommendation; Strength of Evidence Grade C.)
- C linicians should perform uri electromyography (EMG), in combination with CMG with or without PFS in patients with relevant neurologic disease at risk for NGB, in patients with other neurologic disease and elevated PVR, and inpatients with urinary symptoms(11).

Radiologic and Urodynamic Assessment of the Neurogenic Bladder: The current options available to evaluate the neurogenic bladder and upper tracts include ultrasonography (US), fluoroscopy, nuclear medicine studies or urodynamic testing.

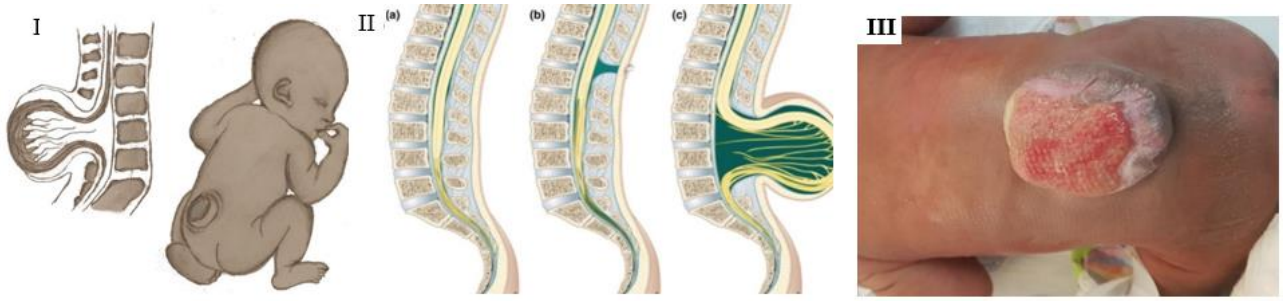
As was urodynamics in children undergoing tetheredcord release (TCR).

Evaluation of Renal Scarring: DMSAVersus US: Regardless of management strategy, the goal to detect early upper tract changes that may precede deterioration is key to long-term prevention of renal failure. Prior series of children with myelodysplasia have demonstrated rates of renal scarring or functional loss of 10-32 % on DMSA nuclear medicine scans . As with spina bifida were evaluated with both DMSA and US modalities to obtain a baseline assessment of renal scarring(12,13,14,15)

Management of the Neurogenic Bladder

Prior to the widespread utilization of CIC for the management of neurogenic bladder, renal failure and urosepsis were common causes of long-term morbidity and mortality.

Fig. 2.Show I. child with open spinal dysraphism. II. Forms of spinal dysraphism, from (Sacco et al., 2019).



(a) normal situation, (b) closed spinal dysraphism (c) myelomeningocele. III. Illustrative myelomeningocele with deficient skin and the exposed
placode comprising primitive neuronal epithelium.

Medical Management

Anticholinergics/Antimuscarinics

Tertiary amines (oxybutynin, tolterodine, darifenacin, solifenacin, and propiverine) are more likely to cross the

blood–brain barrier than quaternary amines propantheline and trospium).

Botulinum-A toxin (BTX-A).

Neuromodulation Treatments

1. **Intravesical electrical stimulation**
2. **Sacral nerve stimulation**

Surgical Reconstruction

When medical and intravesical options fail to provide satisfactory results, surgical reconstruction may be required to maintain low intravesical storage pressure and achieve treatment goals for urinary continence(16).

1. Augmentation Cystoplasty
2. Outcomes of Bladder Neck Procedures Without Augmentation Cystoplasty

Treatment methods used in neurogenic bladder-sphincter dysfunction.

Conservative measures

Clean intermittent catheterization (CIC)

Bladder-inhibiting drugs;

Anticholinergic drugs

b-3 stimulants

Surgical procedures

- Intramural botulinum toxin A
- Bladder augmentation
- Catheterizable stoma (Mitrofanoff)
- Bladder neck surgery and injections
- Vesicostomy/SP catheter
- Other surgical techniques.

MATERIAL AND METHODS

Medical records of 28 patients have been drawn from a computerized database and were evaluated retrospecti-vely. The data included: age, sex, presence of the hydrocephalus. The study protocol was approved by the Ethics Committee, in Azady Teaching Hospital, Kirkuk.

RESULTS

During the study period, 32 patients were admitted because of MMC, 4 refused participation and remaining 28 patients formed the study group. Six patients were seen only one time and then were lost during our follow-up. Two girls aged 5 and 9 years died during the observed period. The cause of death was general infection and dialysis complica-tions. A part of these patients were seen at the illness onset and mostly they were admitted to our hospital later.

Table results1 – Laboratory characteristics of MMC children. S creatinine – serum creatinine. I – data from the first estimation. II – data from the last estimation, eGFR – glomerular filtration rate estimated by Counahan–Barratt equation

All patients	<3 years n = 5	3–6 years n = 8	7–15 years n = 15
Median (minimum–maximum)			
S creatinine I (mg%)	0.27 (0.11–2.49)	0.23 (0.18–0.40) 0.2 (0.16–0.51) 0.27 (0.11–2.49)	
S creatinine II (mg%)	0.31 (0.18–8.57)	0.23 (0.18–0.31) 0.21 (0.18–0.63) 0.34 (0.18–8.57)	
eGFR (ml/min/1.73/m2)	161.25 (4.77–313.92)	160.78 (110.97–193.51) 199.64 (64.84–249.40) 168.92 (4.77–313.90)	
Urine osmolality	693.5 (274–1177)	574 (280–873) 696 (316–931) 732.5 (274–1177)	

Table. results .2		Total
Female/male	112; 60/52	28
Type of delivery cesarean/vaginal	18-Oct	28
BMI Z-score WHO	92; 0,45	28
BMI	94; 17.9	28
Hydrocephalus (%)	95; 82	28

DISCUSSION

Neurosurgeons need to refocus not only on the view under microscope but also on a view outside microscopic field of vision. We should focus on the disorders that affect large numbers of children.Third world countries are facing many problems; socioeconomic, cultural, educational and nutritional that result in congenital anomalies of CNS like neural tube defects (NTD) more frequently than developed societies ' like the USA or Europe. NTD involves entire central nervous system and leads to disability or death. Children are the most valuable individuals in the lives of most people. Nothing else can cause the grief that the death of the child does, and few disasters cause the grief of a permanently brain damaged child. The most common form of neural tube defect is myelomeningocele, a term used synonymously with spina bifida aperta, spinabifida cystica and open neural tube defect(17,18,19,20).

The cause of myelomeningocele is multifactorial and includes genetic predisposition, nutritional deficiencies, particularly folate and zinc, use of anti-epileptic drugs like carbamazepine or valproic acid, diabetes mellitus (type-1), pre-pregnancy obesity and possibility other non medical factors such as agricultural pesticides, radiation, hyperthermia and use of tobacco or drugs. The defect involve neural tissue. Skin over the cystic lesion is not fully developed. The defect size in our series was an average 30.9 cms. In our series all patient had undergone ultrasonography to determine ventricular size and other anomalies like abnormal shaped mid brain; elongated cerebellum and obliteration of cisterna magna, characteristic of Chiari-II malformation(21,22,23).

CT scan of brain and MRI of myelomeningocele were also done in selected cases i.e. 109(26%) of total cases, to exclude associated anomalies and determine the exact location and size of lesion. The role of MRI has been well documented.In our series 155 (37.3%) patients having myelodysplasia were paraplegic and incontinent. We repaired the lesion and placed low-pressure VP shunt, placed low-pressure VP shunt without repair and placed lumbo peritoneal shunt in some cases. Recently cord transaction has been done for repetitive symptomatic tethering to overcome severe pain in the mid thoracic and

lumbar region. The results are encouraging at later stage of life to avoid delayed complications like spasticity and scoliosis.20, 21 In our series 340 (82%) myelomeningoceles were located at thoracolumbar region and 365 (88%) of the cases investigated showed presence of hydrocephalus and Chiari- II malformation. Twenty one (5%) were located in cervical region, and 29 cases (7%) in thoracic region, and non of them was associated with hydrocephalus or other anomalies. Our aim was to assure an independent and productive life for patients with myelomeningocele and their families with reference to normal intelligence, sphincter control, power in lower limbs and other spinal anomalies like scoliosis and kyphosis due to tethering of the cord. We examined different parameters in detail between patients who either developed or came to hospital with complications like ventriculitis and those who did not. As for as normal intelligence is concerned we found ventriculitis as the single most important factor, diagnosed at different stages during the care of patient, either before repair of myelomeningocele, after repair, before VP shunt insertion or after placement of VP shunt. In our series ventriculitis was present in 43 cases (10%); 26 cases (61%) had ventriculitis related to myelomeningocele repair and in 17 cases (4%) due to VP shunt. Organisms found in these cases were usually gastro intestinal tract or skin colonizers. Almost all patients with ventriculitis suffered mental retardation and are under continued follow up. We encountered 16 (3.8%) cases with ruptured myelomeningocele either due to birth trauma, a very thin placode and massive hydrocephalus or due to mishandling by medical professionals. One of the most important issues concerned with management protocol is the optimal timing of myelomeningocele repair. It is generally accepted that repair ideally should be performed 72 hours after birth to avoid ventriculitis.4,5 In our series 16 cases 3.8% were repaired up to 48-72 hours because of CSF leak. In rest of the cases average time of repair was 28 days, due to delayed referral of the cases. All cases had cultures taken from the neural placode and only sterile cases were directly repaired; others were treated with antibiotics before repair. In all infected cases shunt surgery was delayed, until investigation and treatment for ventriculitis was successful. The main purpose of myelomeningocele repair is to protect the functional tissue in the neural placode, to prevent loss of CSF and minimize the risk of meningitis by reconstructing the neural tube and its coverings with a stable soft tissue closure. To avoid complications, use of lumbar periosteal turn over flap and tissue expansion for delayed closure of large myelomeningocele has been advocated.17,6,4 Recently, rectal monitoring during repair of myelomeningocele has been performed to preserve neural tissues.11 In our series all cases were repaired with standard surgical techniques except for large dorsal myelomeningoceles with myelodysplasia. In 52 of 155 cases (33.5%) only a lowpressure VP shunt was inserted without repair of meningocele. There was satisfactory experience 100% shrinkage of myelomeningocele, saving operation time, deterring problem with wound closure due to very thin and inadequate skin, and minimize hospital stay due to poor wound healing(24).

Ongoing Surveillance And Care: myelomeningocele has been described as the most complex birth defect compatible with life. shows the most common findings and their relationship to brain and spinal malformations. Affected children need complex, coordinated care to optimize their health and wellbeing. After the newborn period, the child should be followed on a regular basis and monitored over time in the medical home. Periodic evaluations include:

- Detailed neurologic evaluations of upper and lower extremities. Deterioration of upper extremity function may indicate worsening hydrocephalus due to a problem with the ventricular shunt, a problem with the spinal cord or brainstem (eg, syrinx), or posterior fossa compression from the Chiari malformation. Deterioration of lower extremity function or bowel and bladder function may be a sign of worsening hydrocephalus or tethered spinal cord.
- onitoring for signs and symptoms of increased intracranial pressure from shunt failure . Early recognition of shunt failure or infection is critical.
- Assessment of growth, nutrition, and physical fitness.
- Developmental surveillance and screening, including evaluation of gross motor, fine motor, social, language, and cognitive abilities. Infants born with myelomeningocele should be referred to their local Early Intervention Program by 6 months of age. Children exhibiting development outside the expected norms for this population should have formal psychometric evaluations. Before school entry, all children who have myelomeningocele should undergo a formal psychoeducational evaluation to determine whether they have a learning disability and assess their strengths and weaknesses(25,26)

CONCLUSIONS

The goals in management of the pediatric neurogenic bladder include preservation of the upper and lower urinary tracts and optimization of quality of life.

1. Data of MMC children from are similar to the other countries.
2. Assessment of very early markers in renal function deterioration in neurogenic bladder patients from widespread multicenters research is indicated
3. In our opinion, early diagnostic and treatment procedure especially with early catheterization of MMC children prevent renal failure development

Nowadays, the treatment of choice is initially conservative. Multiple conservativemodalities, i.e pharmacologic agents, medical devices and neuromodulation, should be promoted before undertaking surgical interventions. Intermittent catheterization and drug therapy are usually sufficient for maintaining continence and preserving upper tracts. Surgical procedures should be considered if conservative measures fail to achieve(27,28). Continence between catheterizations or preserve upper tracts. However today the improvement of Quality of life is the final goal(29).

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