

Uronephrological outcomes of patients with neural tube defects

Does a spina bifida clinic make a difference?

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ABSTRACT

الأهداف: مراجعة وظائف الكلى والجهاز البولي لمرضى الصلب المشقوق في العيادة المشتركة للصلب المشقوق (الفتى السحائي).

الطريقة: قمت مراجعة جميع ملفات المرضى بآخر رجعي في العيادة المشتركة للصلب المشقوق من عام 1999م إلى 2009م، مع أقل فترة للمتابعة في العيادة على الأقل سنة واحدة. وتم النظر في ملفات المرضى بالنسبة لمعلومات المرضي وحالة الكلى والجهاز البولي عند أول تقييم في العيادة المشتركة وعند آخر متابعة في العيادة وتم التنظر في معدل ونوع التدخل الجراحي.

النتائج: خلال العشر سنوات كان هناك 188 مريض وجدوا في متابعة مستمرة في العيادة المشتركة من 1999م إلى 2009م. وكان متوسط العمر عند العرض 5.3 ± 3.6 عام درجة انحراف معياري. وكان 109 مرضى (58%) على قسطرة متقطعة نظيفة، وتم حقن 44 (23%) بالبوتكس و 26 (14%) مريضاً تم إعادة الإعمار في المائة حتى آخر فترة متابعة. قدم 66% من المرضى لنا بعد عمر 3 سنوات، حيث كان لهذه المجموعة معدل أعلى بكثير من العمليات الجراحية سواء بالبوتكس $p=0.003$ أو إعادة إعمار المائة $p=0.025$ مقارنة مع أولئك الذين جاءوا في وقت مبكر بالنسبة لنا.

الخاتمة: عيادة الصلب المشقوق متعددة التخصصات جزء أساسي في علاج المرضى الذين يعانون من الصلب المشقوق، من أجل التوصل إلى نتائج آمنة. أدى العرض في وقت مبكر أقل من 3 سنوات في عيادتنا إلى حاجة أقل للتدخل الجراحي مقارنة مع تلك التي عرضت أكثر من 3 سنوات من العمر.

Objectives: To review the uronephrological outcomes of myelomeningocele (MMC) patients attending a Spina Bifida Clinic.

Methods: We retrospectively reviewed the medical records of all patients from the combined Spina Bifida

Clinic, at King Khalid University Hospital, Riyadh, Saudi Arabia between 1999 and 2009 who had at least one year of follow-up with us. We examined their demographic data, uronephrological status at presentation, most recent follow-up, and the rate of surgical intervention.

Results: During the 10-year period, 188 patients were actively followed-up. The mean age at presentation was $5.3 \text{ years} \pm 3.6 \text{ SD}$. At their last follow-up, 109 patients (58%) were using clean intermittent catheterization, 44 (23%) had received Botox® injections, and 26 (14%) had undergone bladder reconstruction. Most (66%) patients were older than 3 years when they presented to us; this group had a significantly higher rate of surgical intervention (Botox® or reconstruction) compared with those who came to us earlier ($p=0.003$ for patients receiving Botox® injections, and $p=0.025$ for patients undergoing bladder reconstruction).

Conclusion: Our multidisciplinary Spina Bifida Clinic is an integral part of MCC management to reach a safe urological outcome. Early presentations to our clinic resulted in a lesser need for surgical intercession compared with those who presented at more than 3 years old.

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Myelomeningocele (MMC) affects one out of every one thousand births, and is the most common cause of pediatric neuropathic bladder. These patients often suffer varying degrees of disability, necessitating the need for a multidisciplinary caregiver team that includes pediatric urologists, neurosurgeons, and orthopedists as well as specialized nurses and social workers.¹ Urological manifestation in patients with MMC is common, resulting in serious negative psychological and medical effects. This mandates early follow-up, and a comprehensive management plan to prevent any irreversible renal damage and stabilize bladder function.² Accordingly, the urological care of these patients was one essential reason for establishing a spina bifida clinic, especially since urological care of children with spina bifida has undergone several important changes in the last 2 decades.³ We established the Spina Bifida Clinic at our institute in 1999; currently, it is a bimonthly clinic, with 188 patients being actively followed-up. Here, we review our experience over the last decade with patients with MMC who were followed in the Spina Bifida Clinic with an emphasis on patients' uronephrological outcomes.

Methods. In this retrospective study, we reviewed the medical records of all patients at our multidisciplinary Spina Bifida Clinic at King Khalid University Hospital, Riyadh, Saudi Arabia between 1999 and 2009 who had at least one year of follow-up with us. All bimonthly Spina Bifida Clinic patients were either delivered at our institution or referred from other centers in the Kingdom. All patients with MMC and at least one year of follow-up were included. Exclusion criteria encompassed patients with other pathologies, such as spinal cord trauma, abnormal bladder function with no neurological localization (for example, posterior urethral valve), and patients with less than one year of follow-up. The urology team evaluated patients using a baseline renal ultrasound, urine test, and renal profile. All patients underwent an urodynamic study to evaluate bladder function by the age of 6 months, or at presentation if referred to us after the age of 6 months. If the kidneys were dilated (hydronephrotic), the urodynamic study revealed a noncompliant bladder, or a urinary tract infection was documented, a voiding cystogram (VCUG) was performed. The following data were collected and evaluated in the current study: patient age at presentation, length of follow-up period, demographic data, uronephrological status at presentation and at last follow-up, current urological active management including surgical interventions, upper urinary tract status, early renal profile, and renal profile at last follow-up. Upper tract deterioration was defined as radiographic evidence of ureteral dilatation or hydronephrosis on ultrasound or new onset or progressive vesicoureteral reflux on VCUG. Abnormal

bladder compliance was defined as an intravesical pressure during filling or leaking in excess of 40 cm H₂O.⁴ Active management was initiated according to results from the reported evaluations and baseline investigations (Figure 1).

The data were collected and analyzed using the Statistical Package for Social Sciences, version 16 (SPSS Inc., Chicago, IL, USA) for simple statistics, and *p*<0.05 was considered significant. Our institute's Ethical Committee approved the study, and we followed the principles of the Declaration of Helsinki.

Results. We analyzed 188 patients from our Spina Bifida Clinic who had at least one year of active follow-up. The mean age at presentation to our clinic was 5.3 years ± 3.6 SD (range: 0.2-14 years), with 97 males (51.5%), and 91 females (48.5%). Most of the families lived near our institution (125 [66.5%]). The mean follow-up period was 3.6 years ± 1.9 SD (range: 1-10 years). Out of 188 patients, 109 (58%) used clean intermittent catheterization (CIC) in conjunction with anticholinergic medications due either to noncompliant bladder and/or urinary incontinence.

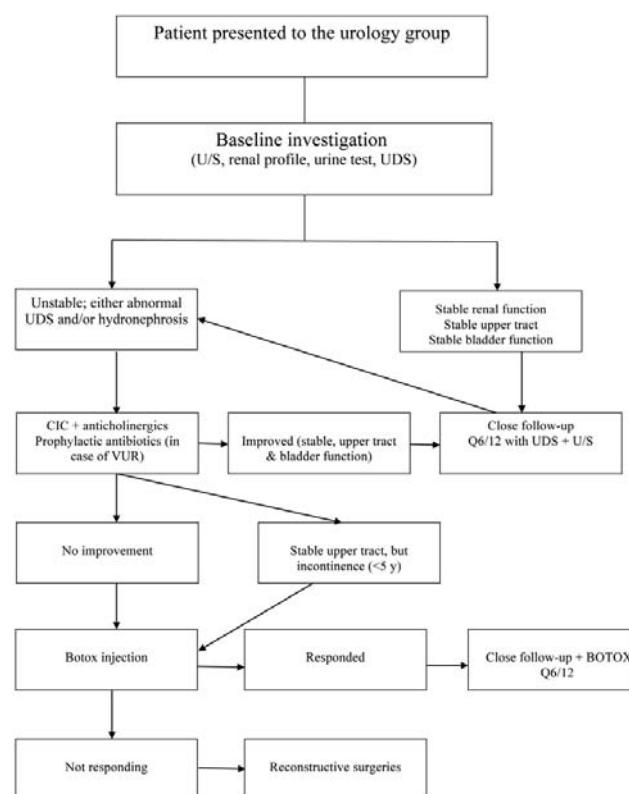


Figure 1 - Urological evaluation and management of patients in the spina bifida clinic. UDS - urodynamic study, U/S - ultrasound, CIC - clean intermittent catheterization, y - years, Q6/12 - every 6 months, VUR - vesicoureteral reflux

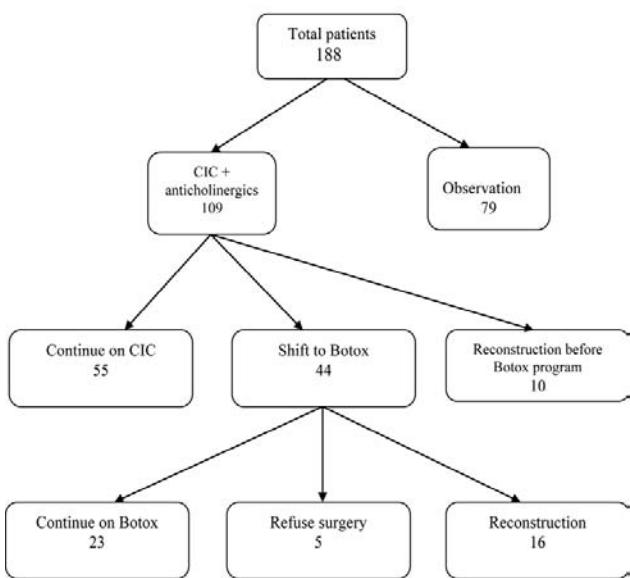


Figure 2 - Total number of patients and different treatment modalities offered to patients during follow-up. CIC - clean intermittent catheterization

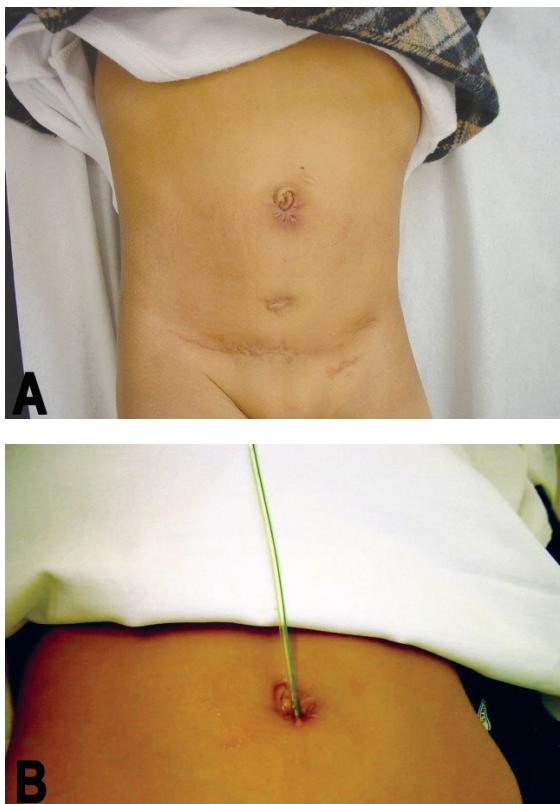


Figure 3 - Patient A) post ileocystoplasty and mitrofanoff procedure B) carrying out self clean intermittent catheterization.

However, 79 patients (42%) showed stable bladder, upper tract, and renal functions and remained under close follow-up observation. Out of the 109 patients, 44 (40.3%) patients had refractory urinary incontinence and/or their upper tract status did not improve with conservative management. Accordingly, their conditions were managed with intradetrusor botulinum toxin injections. Out of the 109 patients, 26 (23.8%) patients underwent bladder reconstruction at their last follow-up, 16 were previously injected with botulinum toxin, and 10 underwent surgical intervention before we started the injection program (Figure 2). At presentation, 160 (85.1%) patients had normal renal function. The mean serum creatinine level was $46.6 \mu\text{mol/L} \pm 40 \text{ SD}$. At the last follow-up, 178 (94.6%) had normal renal function with a mean serum creatinine level of $41.6 \mu\text{mol/L} \pm 32 \text{ SD}$.

Out of 188 patients, 63 (33.5%) patients presented to us before 3 years old, and 125 (66.5%) presented after 3 years old. The older age group had a significantly higher rate of surgical interventions than the younger group. From the older age group, 37 patients underwent botulinum toxin injections, and 22 underwent reconstructive surgery. In contrast, in the younger age group (presentation younger than 3 years) only 7 patients received injections, and 4 patients underwent reconstructive surgery ($p=0.003$ and $p=0.025$). Our patients' overall rate of surgical reconstruction (Figures 3A & 3B) was 13.8% (26 patients); 10 patients underwent surgery before implementation of the injection program and 16 patients did not respond to the injections. Of 188 patients, 44 (23.4%) patients required botulinum toxin injections. In this subgroup, 37 (84%) patients were from the older age group, and 7 (16%) were from the younger age group, a significant difference ($p=0.003$).

Discussion. The urology group, as part of the spina bifida caregiving team, uses urologic care, and management for children with neural tube defects to maintain normal renal functions and achieve a normal social life by maintaining children's urinary and stool continence.⁵ To reach these goals, once the urology team has seen patients, a comprehensive management protocol is developed, a urotherapy nurse introduces the protocol to the family, baseline investigations are performed, and management proceeds according to the schedule in Figure 1. Of our patients, 58% needed CIC either to manage high intravesical pressure or to gain social continence. Despite facing some initial social difficulties, we had excellent outcomes from our CIC Program.⁶

Medical management with CIC and anticholinergics is generally considered effective for preserving renal function and providing safe urinary continence; however, this therapy fails in approximately 10-15%

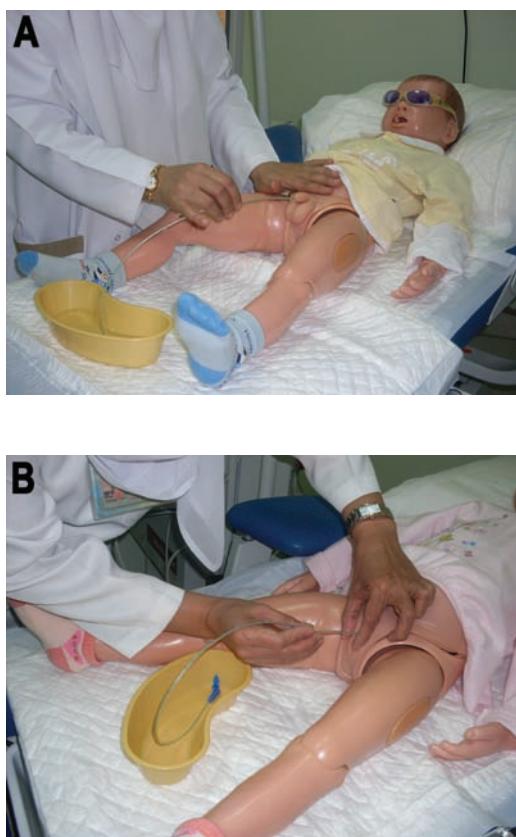


Figure 4 - Figures illustrating teaching sessions of clean intermittent catheterization on models in the urotherapy laboratory: A) male, B) female.

of patients, and surgical reconstruction is the only remaining option.⁷ Recently, intradetrusor injection of botulinum toxin-A (Botox[®]) has been proven efficacious as a second-line treatment for that group of patients.^{7,8} In our analysis of 109 patients, 55 achieved preservation of renal function and safe urinary continence with medical management (CIC teaching and anticholinergics) (Figures 4A & 4B), whereas surgical interventions were indicated in 54 patients (28% of total patients). These results might be explained by the late age of presentation of our patients; approximately 66.5% of our patients presented to our clinic at the age of 3 years or older.

Before 2003, surgical reconstruction was the only solution for patients who did not respond to medical management; however, in 2003 we began using botulinum toxin injections for patients who were nonresponsive to or experienced side effects from standard medical treatments. Out of the 188 patients in this study, 44 (23.4%) patients underwent injections, of which 23 (52.2%) responded well to repeated injections and were able to avoid major surgical reconstruction. Of those patients who did require surgery (26 [13.8%]), they either received it before the injection program was implemented or they did not respond well to injections. Out of the 26 patients who underwent surgical

reconstruction, a significantly higher number of them were from the older group. Similarly, significantly more patients for whom injections were indicated were from the older age group. Clearly, the rate of required surgical interventions was much lower with earlier presentation and start of treatment. This finding supports the need for early, proactive management of patients accompanied by a regularly maintained and well-constructed program to avoid surgical interventions and associated complications.⁹

The study did have some limitations; it was retrospective and had a relatively small number of patients. Despite these limitations; however, the results reinforce the importance of early presentation and follow-up with a spina bifida clinic. Earlier presentation and subsequent strict medical management lowers the rate of surgical intervention. Further large-scale, prospective studies are still needed to confirm these results.

In conclusion, safe kidney function with social continence is achievable for most patients with neurogenic bladder secondary to MMC if they are properly followed-up with a dedicated team in a spina bifida clinic. Although the follow-up can be strenuous and rigorous, we nevertheless strongly recommend early presentation and strict follow-up for these patients in conjunction with early CIC program initiation if necessary.

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