

REVIEW

Mission impossible? Urological management of patients with spinal cord injury during pregnancy: a systematic review

J Pannek¹ and S Bertschy^{2,3}

¹Department of Neuro-Urology, Swiss Paraplegic Center, Nottwil, Switzerland; ²Swiss Paraplegic Research (SPF), Nottwil, Switzerland and ³Department of Health Sciences and Health Policy, University of Lucerne and SPF, Nottwil, Switzerland

Study design: A systematic literature review.

Objectives: To systematically assess the existing knowledge about treatment of neurogenic lower urinary tract dysfunction (NLUTD) in pregnant women with traumatic spinal cord injury (SCI), as urologic management of these patients is mandatory, but no guidelines are available.

Setting: Paraplegic center in Switzerland.

Methods: Studies were identified by electronic search of PubMed and MedLine. Data were pooled and analyzed quantitatively.

Results: The evidence level of all 14 reports (163 patients, 226 pregnancies) included was low. In 13 studies, information was gathered by a retrospective review of the medical records or by questionnaires. In all studies, reported data were incomplete. SCI was cervical in 34.7%, thoracic in 61.2% and lumbar in 4.1% of the pregnant women. In all 34.7% of the women used indwelling catheters, 25% performed intermittent catheterization, 11.5% used the Credé maneuver and 28.8% voided spontaneously. A total of 64% of the patients had at least one symptomatic urinary tract infection (UTI) during pregnancy. UTIs were more common in women with indwelling catheters (100%) than in those performing intermittent catheterization (38.5%), using the Credé technique (17%) or voiding spontaneously (53.3%). One study demonstrated a significant reduction in UTI during pregnancy without complications in mothers or infants.

Conclusion: No evidence-based recommendations can be drawn from the existing literature to guide urologists in the management of NLUTD in pregnant women with SCI. The number of studies is small, and data acquisition and presentation are often inadequate. Thus, further research is urgently needed.
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Keywords: neurogenic lower urinary tract dysfunction; spinal cord injury; urinary tract infection; pregnancy; systematic literature review

Introduction

A traumatic spinal cord injury (SCI) does not impair fertility in women. Following a phase of amenorrhea that occurs in about a third of patients after acute SCI, lasts for about 4 months, and is presumed to be due to a temporary rise in prolactin, reoccurrence of ovulation can be demonstrated, re-establishing the possibility of becoming pregnant for women with SCI.¹

Virtually all patients with a SCI suffer from neurogenic lower urinary tract dysfunction (NLUTD).² The major aim of treatment of these patients is the preservation of renal function. An elevated storage pressure, either due to low bladder compliance or due to neurogenic detrusor over-

activity, is the major risk factor for renal deterioration.³ Therefore, the primary objective of bladder management is to achieve low-pressure urine storage and bladder emptying.⁴ The majority of patients with SCI need regular urologic evaluations and treatment of their bladder dysfunction.⁵

Urinary incontinence and urinary tract infections (UTIs) occur frequently in this group of patients. UTIs are the leading cause of septicemia in patients with spinal cord lesions, and are associated with a significantly increased mortality.⁶ Pregnancy is known to have an impact on the lower urinary tract in neurologically intact women. The risk for bacteriuria, for example, is elevated in pregnant women.⁷ Thus, pregnant women with SCI intuitively should be a high-risk group for UTI.

Without doubt, pregnant women with SCI require urologic care. On the other hand, standard treatment of NLUTD may not be possible during pregnancy, as several drugs, for example, anticholinergic medication, are contraindicated in pregnant women. Therefore, we undertook a systematic

Correspondence: Professor J Pannek, Chefarzt Neuro-Urologie, Schweizer Paraplegiker-Zentrum, Guido A. Zäch Strasse 1, Nottwil, CH 6207, Switzerland.

E-mail: juergen.pannek@paranet.ch

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literature review to assess the current knowledge of urologic management of pregnant women with SCI.

Materials and methods

Evidence acquisition

The systematic review was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement.⁸ We systematically searched electronic databases (PubMed and Medline) for studies published in English or German on the urologic management of pregnant women with SCI (Table 1). No date restrictions were applied. Search terms were customized to each database and involved combining key word searches for a list of adjustment terms, terms describing NLUTD and the term construct to describe 'spinal cord injury'.

Abstracts of all identified studies were independently reviewed by the authors and studies reporting on the urologic management of pregnant women with NLUTD were reviewed in full text.

Data extraction

Data from eligible reports were extracted by the authors. Information from each study that was relevant to the research question and in line with inclusion criteria was extracted and tabulated. The extracted data comprised publication data, study type, level of evidence, number of patients, age, number of pregnancies, urologic management and outcome. The level of evidence and type of studies were classified according to the Oxford Center of Evidence-Based Medicine criteria (<http://www.pdptoolkit.co.uk/Files/ebm/cebm/Doing%20ebm/levelsofevidencetable.htm>).

Synthesis

The extracted data were analyzed quantitatively. The information regarding urologic management extracted from all reports available was pooled and descriptive statistics were performed.

Statistics

For statistical analyses, a statistics and graphics management system (STATA, Santa Monica, CA, USA) was used. Owing to the paucity of data, merely descriptive statistical analyses were performed.

Results

Overview

After removing duplicates, we retrieved 228 articles. An initial review of these records found that 187 did not address the research question. However, 41 were potentially relevant. Full versions of these articles were obtained and reviewed against inclusion criteria. Uncertainties with regard to whether a study met inclusion criteria were resolved through discussion between the authors. After reviewing all abstracts and the full text of any study reporting on the urologic management of pregnant women with NLUTD due to SCI,

Table 1 Search strategy

1	Spinal cord
2	Injur*
3	Lesion
4	Trauma*
5	Damage*
6	2 OR 3 OR 4 OR 5
7	1 AND 6
8	Tetrapleg*
9	Parapleg*
10	Quadripleg*
11	Quadrupleg*
12	8 OR 9 OR 10 OR 1
13	12 OR 7
14	Pregnan* [MeSH]
15	Pregnancy
16	Motherhood
17	Mother*
18	Parent*
19	14 OR 15 OR 16 OR 18
20	13 AND 19
21	Women [MeSH]
22	Woman
23	Female
24	21 OR 22 OR 23
25	20 AND 24
26	Neurogenic lower urinary tract dysfunction
27	Neurogenic bladder
28	Detrusor overactivity
29	Detrusor hyperreflexia
30	Detrusor sphincter dysynergia
31	Urinary retention
32	Urinary bladder
33	26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32
34	33 AND 25
35	Urinary tract infection
36	25 AND 35
37	Electric stimulation therapy [MeSH]
38	Sacral nerve stimulation
39	Sacral neuromodulation
40	37 OR 38 OR 39
41	25 AND 40
42	Sacral deafferentation
43	SARS/SDAF
44	Anterior root stimulation
45	Brindley
46	42 OR 43 OR 44 OR 45
47	25 AND 46
48	Anticholinergic*
49	Antimuscarinic*
50	48 OR 49
51	25 AND 50
52	Bladder augmentation
53	Ileum augmentation
54	52 OR 53
55	25 AND 55
56	Botulinum toxin
57	Botox
58	56 OR 57
59	25 AND 59 60 catheter*
61	Intermittent
62	Suprapubic
63	Indwelling
64	60 OR 61 OR 62 OR 63
65	25 AND 64
66	α blocker
67	25 AND 66

15 publications were identified that matched the aforementioned criteria. One paper was a follow-up of a previous publication, including the entire study population of the

initial publication. Thus, 14 articles identified through the search were ultimately included in the review (Figure 1).

Study and patient characteristics

The level of evidence of the included studies ranged from 2b to 4 (Table 2). One was a prospective cohort study,²² nine were retrospective case series^{9–14,16,18,21} and four were case reports.^{15,17,19,20} In the case series and the case reports, information was gathered by a retrospective review of the medical records or by interviews of women with SCI who have borne children (Table 2).

Overall, 163 women with 226 pregnancies were enrolled. The number of pregnancies ranged from 1 to 5, with an average of 1.4 pregnancies per woman. The mean age ranged from 20 to 34.66 years. The mean duration of the SCI was between 2.5 and 15.7 years. In all 34 patients had cervical lesions, 60 had thoracic injuries and 4 patients had lumbar lesions. In the remaining 65 patients, no information about the level of SCI was given. SCI was complete in 29 patients and incomplete in 22 patients; in 112 patients, no information about completeness of SCI was available.

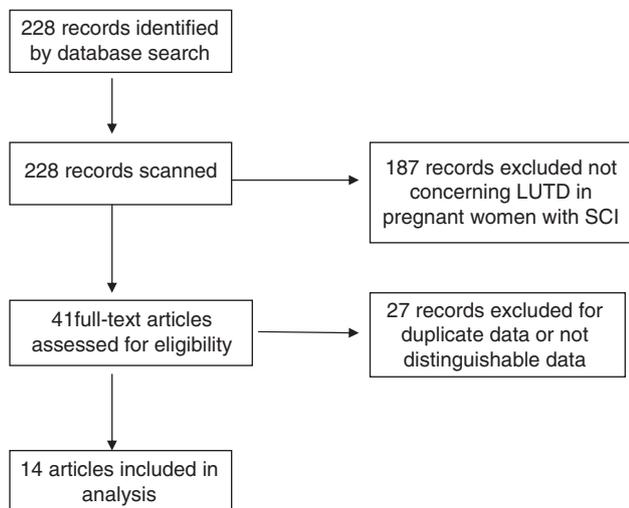


Figure 1 Diagram of the review process.

Table 2 Summary of the studies included in the review

Study	Year of publication	LoE	Study type	No. of patients	No. of pregnancies
Baker <i>et al.</i> ⁹	1992	4	Retrospective case series	11	13
Craig ¹⁰	1990	4	Retrospective case series	9	13
Cross <i>et al.</i> ¹¹	1992	4	Retrospective case series	22	33
Feyi-Waboso ¹²	1992	4	Retrospective case series	8	8
Jackson <i>et al.</i> ¹³	1999	4	Retrospective case series	66	101
Kulkarni <i>et al.</i> ¹⁴	1992	4	Retrospective case series	6	6
McGregor <i>et al.</i> ¹⁵	1985	4	Case report	1	1
Rageth <i>et al.</i> ¹⁶	1986	4	Retrospective case series	13	17
Rossier <i>et al.</i> ¹⁷	1969	4	Case report	1	1
Skowronski <i>et al.</i> ¹⁸	2008	4	Retrospective case series	5	7
Sziller <i>et al.</i> ¹⁹	1973	4	Case report	1	1
Tsoutsoplides ²⁰	1982	4	Case report	1	2
Wanner <i>et al.</i> ²¹	1987	4	Retrospective case series	13	17
Salomon <i>et al.</i> ²²	2009	2b	Prospective cohort study	6	6
				163	226

Abbreviation: LoE, level of evidence.

Mode of bladder management

In 52 women, the mode of bladder evacuation was described. Of these, 18 women (34.7%) used indwelling (transurethral or suprapubic) catheters, 13 (25%) performed intermittent catheterization, 6 (11.5%) used the Credé maneuver and 15 (28.8%) voided spontaneously.

UTIs

One case study based on retrospective patients' recollection stated that UTIs were more frequent in pregnancies post injury (45.5%) than in pregnancies before SCI (8.2%).¹³

In 10 reports covering 139 patients, data about UTIs were available. Of these, 89 (64%) patients had at least one symptomatic UTI, leading to eight hospitalizations. In five cases, pyelonephritis was documented, and one case of septicemia leading to preterm labor was described. Recurrent UTIs were stated in 29 patients; four women suffered from chronic UTI. However, no clear-cut definitions were available for the terms 'UTI', 'recurrent UTI' and 'chronic UTI'. All UTIs required antibiotic treatment. In 15 patients, prophylactic antibiotic treatment was established. As neither indications for nor results of prophylactic antibiotic treatment were clearly stated, no conclusions regarding the usefulness of this treatment could be drawn.

One study with six patients prospectively evaluated the usefulness of a regimen called 'weekly oral cycling antibiotic'. The rate of UTI could be significantly reduced from 6 UTIs per patient per year before pregnancy to 0.4 UTI per patient per year during pregnancy without complications in mothers or infants.²²

Correlation between mode of bladder evacuation and UTIs

All 18 women with indwelling catheters experienced at least one UTI during pregnancy (100%). Of the 13 women with intermittent catheterization, five patients developed UTI (38.5%), whereas UTIs were reported in 1 of the 6 women performing the Credé technique (17%) and in 8 of the 15 patients voiding spontaneously (53.3%).

Other urologic complications

Quantifiable urologic complications described in the retrieved records were four bladder stones newly diagnosed during pregnancy. Other complications, such as incontinence, were mentioned, but not quantified. A single study with 66 patients, of which 40% had an indwelling catheter, reported leakage around the indwelling catheter in 15%, bladder spasms being so significant that catheters were expelled in 9.1% and there was a necessity to change the mode of bladder management in 25%. However, no details were reported.

Discussion

Despite the fact that an increasing number of women with SCI are biologically able to conceive children, the implications of pregnancy on urologic treatment in women with SCI have not yet been assessed in a systematic manner. We found that the level of evidence was low for all studies that addressed this issue. This is not surprising, as the number of pregnant women with SCI is rather low; therefore, a randomized prospective study with an adequate number of subjects is difficult to initiate. Furthermore, randomized prospective studies in pregnant women raise severe ethical concerns. However, it was surprising to us that the quality of the existing data was poor. Only a single study has been specifically designed to evaluate urologic problems during pregnancy.²² In all studies, documentation of even basic data, such as age, medical treatment of NLUTD, mode of bladder evacuation and level of injury, was incomplete. Only one study¹² stated that the mode of bladder management remained unchanged during pregnancy. Thus, data regarding timing and rationale for the bladder management changes were lacking.

The data we retrieved mainly addressed the rate of UTI and the mode of bladder management. Based on the available data, however, no sound conclusions are possible. The rate of UTI during pregnancy in women with SCI seems to be rather high (64%), but the validity of these data is hampered by the varying definitions of the term 'UTI'. As UTIs are known to be a risk factor for pyelonephritis and low birthweight, and a Cochrane review in pregnant women without SCI demonstrated that antibiotic treatment resulted in a reduced incidence of these complications,²³ treatment of UTI in pregnant women with UTI should be considered, although treatment of asymptomatic bacteriuria is usually not indicated in patients with SCI.⁶

For prevention of UTI in pregnant women with UTI, a very small prospective case study suggests that using a weekly oral cycling antibiotic program may significantly reduce the incidence of UTI,²² but the data are not sufficient to allow an evidence-based recommendation.

Although the rate of UTI in women with indwelling catheters is higher than in those performing any other mode of bladder evacuation, the risks and benefits of indwelling catheterization during pregnancy in women with SCI cannot be answered based on the data of the review. Even though the lowest UTI rate was described in women using the Credè

maneuver, owing to the small number of patients, it is not possible to give any evidence-based recommendation for the use of a certain bladder evacuation technique to reduce UTI rates.

The paucity of data is astonishing and disappointing indeed, as the number of women with SCI getting pregnant seems to be increasing.²⁴ On one hand, it is evident that NLUTD needs to be treated to prevent secondary complications.⁴ On the other hand, it is well known that a large number of treatment options for lower urinary tract dysfunction are either contraindicated in pregnancy (for example, certain anticholinergic drugs), or their use has not been thoroughly studied in this condition.

For example, no data are available with regard to the safety of anterior root stimulation, a technique exclusively used in SCI patients, during pregnancy. Regarding botulinum toxin A, a questionnaire-based survey, including 16 women²⁵ and 4 additional case reports,^{26–29} described the use of botulinum toxin A treatment up to a dose of 300 i.u. Botox during pregnancy for various indications without noted complications for the patient or the child.

For sacral neuromodulation in pregnant women, only case studies with a small number of patients exist. In summary, it was advised to deactivate the device during pregnancy, but no negative implications of sacral neuromodulation on the course of the pregnancy have been described.³⁰

For bladder augmentation, the largest case series comprised 15 pregnant women without SCI. In all 60% of the patients suffered from pyelonephritis, but continence was preserved and pregnancies were possible without major adverse events.³¹

One cannot draw any conclusions for the management of pregnant women with SCI based on these reports, as the specifics of patients with SCI are not taken into consideration. Therefore, well-designed clinical studies are needed to be able to adequately counsel pregnant women with SCI. Until today, it is virtually impossible to give any recommendations for the urologic management of women with SCI during pregnancy based on the results of a systematic literature review.

Conflict of interest

The authors declare no conflict of interest.

References

- 1 Reame NE. A prospective study of the menstrual cycle and spinal cord injury. *Am J Phys Med Rehabil* 1992; 71: 15–21.
- 2 de Groat WC, Kawatani M, Hisamitsu T, Cheng CL, Ma CP, Thor K *et al.* Mechanisms underlying the recovery of urinary bladder function following spinal cord injury. *J Auton Nerv Syst* 1990; 30 (Suppl): 71–77.
- 3 Gerridzen RG, Thijssen AM, Dehoux E. Risk factors for upper tract deterioration in chronic spinal cord injured patients. *J Urol* 1992; 147: 416–418.
- 4 Stöhrer M, Blok B, Castro-Diaz D, Chartier-Kastler E, Del Popolo G, Kramer G *et al.* EAU guidelines on neurogenic lower urinary tract dysfunction. *Eur Urol* 2009; 56: 81–88.
- 5 Nosseir M, Hinkel A, Pannek J. Clinical usefulness of urodynamic assessment for maintenance of bladder function in patients with spinal cord injury. *Neurourol Urodyn* 2007; 26: 228–233.

- 6 Biering-Sørensen F, Bagi P, Høiby N. Urinary tract infections in patients with spinal cord lesions: treatment and prevention. *Drugs* 2001; **61**: 1275–1287.
- 7 Holroyd-Leduc JM, Straus SE. Management of urinary incontinence in women: scientific review. *JAMA* 2004; **291**: 986–995.
- 8 Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6**: e1000097.
- 9 Baker ER, Cardenas DD, Benedetti TJ. Risks associated with pregnancy in spinal cord-injured women. *Obstet Gynecol* 1992; **80**: 425–428.
- 10 Craig DI. The adaptation to pregnancy of spinal cord injured women. *Rehabil Nurs* 1990; **15**: 6–9.
- 11 Cross LL, Meythaler JM, Tuel SM, Cross AL. Pregnancy, labor and delivery post spinal cord injury. *Paraplegia* 1992; **30**: 890–902.
- 12 Feyi-Waboso PA. An audit of five years' experience of pregnancy in spinal cord damaged women. A regional unit's experience and a review of the literature. *Paraplegia* 1992; **30**: 631–635.
- 13 Jackson AB, Wadley V. A multicenter study of women's self-reported reproductive health after spinal cord injury. *Arch Phys Med Rehabil* 1999; **80**: 1420–1428.
- 14 Kulkarni S, Morgan OS. Pregnancy outcome in paraplegic women. *W Indian Med J* 1992; **41**: 99–100.
- 15 McGregor JA, Meeuwse J. Autonomic hyperreflexia: a mortal danger for spinal cord-damaged women in labor. *Am J Obstet Gynecol* 1985; **151**: 330–333.
- 16 Rageth JC, Wanner M, Iljazovic S, Heinzl S. Schwangerschaft, Geburt und Wochenbett bei Paraplegikerinnen. *Geburtshilfe Frauenheilkd* 1986; **46**: 536–540.
- 17 Rossier AB, Ruffieux M, Ziegler WH. Pregnancy and labour in high traumatic spinal cord lesions. *Paraplegia* 1969; **7**: 210–216.
- 18 Skowronski E, Hartman K. Obstetric management following traumatic tetraplegia: case series and literature review. *Aust New Zeal J Obstet Gynaecol* 2008; **48**: 485–491.
- 19 Sziller O, Novoszel T. ber die Schwangerschaft und Entbindung gelähmter Frauen. *Zentralblatt Gynakol* 1973; **95**: 1589–1594.
- 20 Tsoutsoplides GC. Pregnancy in paraplegia: a case report. *Int J Gynaecol Obstet* 1982; **20**: 79–83.
- 21 Wanner MB, Rageth CJ, Zäch GA. Pregnancy and autonomic hyperreflexia in patients with spinal cord lesions. *Paraplegia* 1987; **25**: 482–490.
- 22 Salomon J, Schnitzler A, Ville Y, Laffont I, Perronne C, Denys P *et al.* Prevention of urinary tract infection in six spinal cord-injured pregnant women who gave birth to seven children under a weekly oral cyclic antibiotic program. *Int J Infect Dis* 2009; **13**: 399–402.
- 23 Smaill F, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. *Cochrane Database Syst Rev* 2007 CD000490.
- 24 Ghidini A, Simonson MR. Pregnancy after spinal cord injury: a review of the literature. *Top Spinal Cord Inj Rehabil* 2011; **16**: 93–103.
- 25 Morgan JC, Iyer SS, Moser ET, Singer C, Sethi KD. Botulinum toxin A during pregnancy: a survey of treating physicians. *J Neurol Neurosurg Psychiatry* 2006; **77**: 117–119.
- 26 Li Yim JF, Weir CR. Botulinum toxin and pregnancy—a cautionary tale. *Strabismus* 2010; **18**: 65–66.
- 27 Wataganara T, Leelakusolvong S, Sunsaneevithayakul P, Vantanasiri C. Treatment of severe achalasia during pregnancy with esophagoscopy injection of botulinum toxin A: a case report. *J Perinatol* 2009; **29**: 637–639.
- 28 De Oliveira Monteiro E. Botulinum toxin and pregnancy. *Skinmed* 2006; **5**: 308.
- 29 Newman WJ, Davis TL, Padaliya BB, Covington CD, Gill CE, Abramovitch AL *et al.* Botulinum toxin type A therapy during pregnancy. *Mov Disord* 2004; **19**: 1384–1385.
- 30 Wiseman OJ, v d Hombergh U, Koldewijn EL, Spinelli M, Siegel SW, Fowler CJ. Sacral neuromodulation and pregnancy. *J Urol* 2002; **167**: 165–168.
- 31 Hill DE, Kramer SA. Management of pregnancy after augmentation cystoplasty. *J Urol* 1990; **144**: 457–459.