

ORIGINAL ARTICLE

# Pregnancy in spinal cord-injured women, a cohort study of 37 pregnancies in 25 women

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**Study design:** A retrospective observational study.

**Objective:** To describe specificities of pregnancy in a traumatic spinal cord-injured (SCI) population managed by a coordinated medical care team involving physical medicine and rehabilitation (PMR) physicians, urologists, infectious diseases' physicians, obstetricians and anaesthesiologists.

**Setting:** NeuroUrology Department in a University Hospital, France.

**Methods:** All consecutive SCI pregnant women managed between 2001 and 2014 were included. A preconceptional consultation was proposed whenever possible. Obstetrical and urological outcomes, delivery mode and complications were reported.

**Results:** Overall, thirty-seven pregnancies in 25 women, of a mean age of  $32 \pm 4$  years, were included. Thirty-five children were born alive (three miscarriages, a twin pregnancy) without complications except for a case of neonatal respiratory distress in premature twins born at 33 weeks. The mean birth weight was  $2979 \pm 599$  g. Twenty-one (57%) pregnancies benefited from preconceptional care. A weekly oral cyclic antibiotic programme was prescribed in 28 (75%) pregnancies. The main complications during pregnancy included pyelonephritis (30%), lower urinary tract infections (UTI) (32%), pressure sores (8.8%) and prematurity (12% deliveries before 37 weeks, with only one delivery before 36 weeks). Two patients suffered from autonomic dysreflexia, one with serious complication (brain haematoma). Caesarean sections were performed for 68% of deliveries (23/34) to prevent syringomyelia deterioration ( $n = 10$ ), stress urinary incontinence aggravation ( $n = 3$ ) or for obstetrical reasons ( $n = 7$ ).

**Conclusions:** Mothers' and infants' outcomes were satisfying after pregnancy in SCI women, but required many adjustments. Pregnancy must be prepared by a preconceptional consultation, and managed by a multidisciplinary team involving specialists of neurological disability and pregnancy.

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## INTRODUCTION

Spinal cord injury (SCI) has been reported to have an incidence of 1200 new cases per year in France (19.4 new cases per million inhabitants) and a prevalence of 50 000.<sup>1</sup> Trauma represents more than 50% of causes of SCI. Moreover, 50% of SCI occurs in patients aged between 15 and 25 years, with 15–20% being women.<sup>2</sup> Fertility ability in women is not reduced after SCI.<sup>3,4</sup> However, the fertility rate per woman is lower compared with that in the general population.<sup>4,5</sup>

A few studies, presented in Table 1 (non-exhaustive list), have assessed the issue of pregnancy among SCI patients (many retrospective series, one small prospective observational study, two reviews).

The congenital malformation rate is not higher than that in the general population.<sup>3,4</sup> Neonatal mortality rate was not higher in the most recent studies.<sup>4,5,8,9,11,12</sup> However, high rates of maternal and infant complications secondary to associated disabilities were reported. UTI was the most frequent complication in SCI pregnant women, as was present in most studies: 45–100% had lower UTI, 75% had repeated urinary infections<sup>4,12</sup> and 23–31% had pyelonephritis.<sup>8,12</sup> Urologic management was more challenging: one-fourth of the

women reported the need to change their usual bladder management method during pregnancy, and 27–70% had to increase their number of intermittent catheterizations per day.<sup>4,11</sup>

Autonomic dysreflexia was reported in 60% of pregnant women with spinal cord lesion above T6.<sup>8,9</sup> This very common complication in high SCI patients (85% of patients with injury at or above T6 (ref. 15)) can be a life-threatening situation: two cases of cerebral haemorrhage during labour were reported<sup>16,17</sup> and can appear specifically during labour.

The other complications were pressure sores (6–15%),<sup>4,7–10</sup> worsening of spasticity (which may indicate the beginning of labour) and greater constipation.<sup>4,5,8</sup> Few cases of deep vein thrombosis or pulmonary embolisms were reported, despite cumulative risk for hypercoagulable state during pregnancy and relative immobility due to SCI.<sup>13</sup>

For a newborn, the main complications were prematurity (13–21%)<sup>4,5,9,10</sup> and low birth weight, and there were trends for more cases of fever, jaundice, or blood transfusion.<sup>4</sup>

The aim of this work was to describe specificities of pregnancy in a traumatic SCI population managed by coordinated medical care

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**Table 1 Summary of the studies about pregnancy in SCI women**

Authors	Year of publication	Study type	No. of pregnancy
Salomon <i>et al.</i> <sup>5</sup>	2009	Prospective	7
Robertson and Guttman <sup>7</sup>	1963	Retrospective	11+22
Charlifue <i>et al.</i> <sup>5</sup>	1992	Retrospective	78
Baker <i>et al.</i> <sup>8</sup>	1992	Retrospective	13
Cross <i>et al.</i> <sup>9</sup>	1992	Retrospective	33
Westgren <i>et al.</i> <sup>10</sup>	1993	Retrospective	49
Jackson <i>et al.</i> <sup>4</sup>	1999	Retrospective	101
Galusca <i>et al.</i> <sup>11</sup>	2015	Retrospective	20
Guerby <i>et al.</i> <sup>12</sup>	2015	Retrospective	17
Baker <i>et al.</i> <sup>13</sup>	1996	Review	Not specified
Pannek <i>et al.</i> <sup>14</sup>	2011	Review	226

involving PMR physicians, obstetricians, anaesthesiologists and urologists.

## MATERIALS AND METHODS

A retrospective observational study included all consecutive pregnant patients with a spinal cord injury managed in a University Hospital between March 2001 and September 2014. The following data were collected: neurological status, neuro-urological status before and during pregnancy, obstetrical and neonatal situation, and postpartum complications.

A preconceptional consultation was proposed as often as possible. The main point was neurogenic bladder management during pregnancy: usual follow-up (clinical, biological, urodynamic and radiologic assessment) and adaptation of care for pregnancy. For patients treated with intradetrusor injections of botulinum toxin, injections were stopped, and a minimum of 6 months between the last injection and the beginning of pregnancy was recommended. Anticholinergic drugs used in first intention were oxybutynin and/or trospium, because there are more data to support their safety during pregnancy<sup>18</sup> than with the more recent anticholinergic drugs. A weekly oral cyclic antibiotic (WOCA) was prescribed to prevent urinary tract infection (UTI), according to Salomon's protocol.<sup>6</sup> During the preconceptional consultation, education on prevention of complications was imparted (risk for pressure sore, autonomic dysreflexia and prematurity) and spinal cord MRI was performed to search for a syringomyelia. Advice regarding the type of delivery, anaesthesia and follow-up was given. A review of all drugs used by the patients to control other disabilities (spasticity, pain and constipation) was conducted to reduce iatrogenicity. Patients were referred to a maternity unit with experience in neurological disability, and care coordination with obstetricians and anaesthetists was prepared.

Data are presented as mean  $\pm$  s.d. The  $\chi^2$  test was used.

## RESULTS

Overall, 37 pregnancies in 25 SCI women, of mean age  $32 \pm 4$  years, were included. Fifteen women were followed for one pregnancy, 8 for 2 pregnancies and two for three pregnancies. Baseline characteristics of patients are summarised in Table 2.

Spinal cord injury was post-traumatic in 23 women (16 public highway accidents, 2 ski accidents, 2 parachute accidents, one climbing accident, one ballistic trauma and one unknown) and secondary to herniated disc in 2 women. The average length between spinal cord injury and beginning of pregnancy was  $10 \pm 5$  years. There was no pressure sore, nor was an intrathecal baclofen pump used to treat spasticity, in this population.

All kidney ultrasounds were normal except for one with renal lithiasis. Mean creatinine clearance, measured with 24-h urine collection, was  $105 \pm 32$  ml min<sup>-1</sup> (from 52 to 158 ml min<sup>-1</sup>). There were 24% women with underactive or normal bladder and 76% with

**Table 2 Baseline characteristics of patients**

	Number of women (%)	Number of pregnancies (%)
Total population	25 (100)	37 (100)
<i>Neurological characteristics</i>		
Level of lesion		
Cervical	2 (8)	4 (11)
Thoracic at or above T6	7 (28)	10 (27)
Thoracic below T7	9 (36)	14 (38)
Lumbar or sacral	7 (28)	9 (24)
ASIA <sup>a</sup> classification		
A	13 (52)	22 (59)
B	2 (8)	3 (8)
C, D or E	9 (36)	11 (30)
Unknown	1 (4)	1 (3)
Syringomyelia	5 (20)	10 (27)
<i>Neuro-urological characteristics before pregnancy</i>		
Bladder evacuation		
Intermittent catheterization	20 (80)	31 (84)
Spontaneous voiding	5 (20)	6 (16)
Indwelling urinary catheter	0 (0)	0 (0)
Noncontinent urinary diversion	0 (0)	0 (0)
Augmentation cystoplasty	3 (12)	5 (14)
Continence		
Total		24 (65)
Incomplete <sup>b</sup>		9 (24)
Data missing		4 (11)
Bladder function		
Underactive or normal bladder		9 (24)
Overactive bladder		28 (76)
Anticholinergic drugs		20 (54)
Oxybutynin		9 (24)
Trospium		4 (11)
Oxybutynin and trospium		7 (19)
Botulinum toxin		15 (41)
Balance of bladder function		
Well-balanced bladder		20 (54)
Unbalanced bladder		11 (30)
Data missing		6 (16)
Preconceptional consultation		21 (57)
<i>Neuro-urological characteristics during pregnancy</i>		
WOCA <sup>c</sup> programme		28 (76)
Balance of bladder function		
Well-balanced bladder		19 (52)
Unbalanced bladder		9 (24)
Data missing		9 (24)

<sup>a</sup>American Spinal Injury Association.

<sup>b</sup>At least one urinary leakage.

<sup>c</sup>Weekly oral cyclic antibiotic.

overactive bladder, controlled or not by anticholinergic, all using chronic intermittent catheterization (CIC). Fifteen patients were treated with detrusor injection of botulinum toxin before pregnancy. The delay between the last injection and beginning of pregnancy ranged from 0 to 120 months. On the basis of clinical criteria (perfect continence) and urodynamic test (low-pressure storage below 40cm H<sub>2</sub>O), there were 54% women with well-balanced bladder and 30% with unbalanced bladder before pregnancy (data were missing for 16%).

**Table 3 Antenatal complications, perinatal outcome and postpartum complications**

	No. of pregnancies (%)	No. of deliveries (%)	No. of deliveries with SCI at or above T6 (%)
	37 (100)	34 (100)	13 (100)
Miscarriages	3 (8)		
<i>Antenatal complications</i>			
Pyelonephritis	11 (30)		
Lower UTI <sup>a</sup> (one or more)	12 (32)		
Pressure sores		3 (9)	2 (15)
Dysreflexia		1 (3)	1 (7.7)
Gestational diabetes		1 (3)	1 (7.7)
Prematurity (< 37 weeks)		4 (12)	3 (23)
36 weeks		3 (9)	3 (23)
33 weeks		1 (3)	0 (0)
Vaginal delivery		11 (32)	3 (23)
Caesarean		23 (68)	10 (77)
Syringomyelia		10 (30)	4 (31)
Stress urinary incontinence		3 (9)	0 (0)
Obstetrical reasons		7 (20)	4 (31)
Unknown reason		3 (9)	2 (15)
<i>Anaesthesia</i>			
Yes		28 (82)	12 (92.3)
Spinal or epidural		24 (70)	11 (85)
General		4 (12)	1 (7.7)
No		4 (12)	0 (0)
Unknown		2 (6)	1 (7.7)
<i>Postpartum complications</i>			
Dysreflexia		2 (6)	2 (15)
Brain haematoma		1 (3)	1 (8)
UTI <sup>a</sup>		5 (15)	3 (23)
Deep vein thrombosis		1 (3)	0 (0)
Lung infection		1 (3)	0 (0)
Post-antibiotic colitis <sup>b</sup>		1 (3)	0 (0)
Psychiatric disorder		1 (3)	1 (8)

<sup>a</sup>Urinary tract infection.

<sup>b</sup>Post-antibiotic pseudomembranous colitis with *Clostridium*.

All patients were followed up by the NeuroUrology Department (involving PMR and urologists), an infectious diseases' physician and obstetric team, but only 57% benefited from preconceptional care. A WOCA programme was prescribed in 75% of pregnancies. During pregnancy, none of the patients needed to change the usual bladder management method; there were 52% with clinically well-balanced bladder and 24% with clinically unbalanced bladder (urine leakage, more frequent CIC and more voiding dysfunction for women voiding spontaneously). Data were missing for 24%.

Thirty-five children were born alive (there were three miscarriages and a twin pregnancy) without complications except for two cases of neonatal respiratory distress in a context of prematurity at 33 weeks (twins). Evolution was favourable with neonatal resuscitation care for the twins (ventilator weaning in 8 h), and there was no early neonatal complication in the other children. The mean birth weight was 2979 ± 599 g.

**Table 4 WOCA<sup>a</sup> and urinary infection**

	WOCA +	WOCA –		WOCA +	WOCA –
Pyelonephritis +	5	3	Lower UTI +	11	1
Pyelonephritis –	23	6	Lower UTI –	17	8
	NS <sup>b</sup> ( <i>P</i> = 0.597)			NS <sup>b</sup> ( <i>P</i> = 0.373)	

<sup>a</sup>Weekly oral cyclic antibiotic.

<sup>b</sup>Nonsignificant.

Antenatal complications, perinatal outcome and postpartum complications are summarised in Table 3. The main complications during pregnancy were pyelonephritis (30%) and lower UTI (32%), sometimes with recurrent infections. There was no relation between WOCA programme use and urinary infection, with or without fever (Table 4). The other complications were three miscarriages (2 during the first trimester and one at 21 weeks, all undetermined causes), prematurity (12% of deliveries before 37 weeks, with only one delivery before 36 weeks) and pressure sores (8.8%). Anaesthesia during labour was given to all patients with a spinal injury level at or above T6, mainly by means of an epidural catheter, which was maintained for 24–48 h, to prevent autonomic dysreflexia. Only two patients (15% of deliveries with SCI at or above T6) suffered from autonomic dysreflexia: before delivery and during postpartum in one, and during postpartum in the other patient with a serious complication (brain haematoma). Caesarean sections were performed for 68% of deliveries (23/34) to prevent syringomyelia deterioration (*n* = 10) or stress urinary incontinence aggravation (*n* = 3), or for obstetrical reasons (*n* = 7).

The most serious postpartum complication was a frontal brain haematoma, revealed by a mild aphasia three days after a caesarean section in a patient with autonomic dysreflexia despite prolonged epidural anaesthesia of 48 h, but with a too early decrease in the dosage of anaesthetics. Neurologic outcome was favourable. Usual bladder management method was preserved postpartum.

## DISCUSSION

This retrospective observational study reports a consecutive series of 37 pregnancies in 25 SCI patients. Despite some complications as in previous studies (pyelonephritis, lower UTI, dysreflexia and pressure sores), mothers' and infants' outcomes were satisfying: the prematurity rate was low and there were no neonatal complications, except for a twin pregnancy born at 33 weeks.

The UTI rate was low (32%) compared with that in other studies (45 to 100%), but the pyelonephritis rate was still high (30%). There were two different contexts to explain these eleven cases of pyelonephritis (all had overactive detrusor muscle and were using a CIC): half happened in patients with a neurological bladder that was well monitored but with very high risks, especially with botulinum toxin discontinuation for pregnancy, or in patients already under a double anticholinergic drug regimen. The five other pyelonephritis cases were probably favoured by an overactive bladder that was poorly treated (patients with poor compliance to treatment or follow-up). These urinary infections explain in large part the 12% prematurity, which remains low compared with that in other studies (13–21%),<sup>4,5,9,10</sup> and without neonatal complications except for the twin pregnancy.

Asymptomatic bacteriuria is frequent in patients using CIC (70%), but is usually with no consequence when low-pressure storage and complete voiding are obtained, and does not require preventive treatment by chronic administration of antibiotics aside from during

pregnancy.<sup>19</sup> However, UTI are the most frequent complication in this population.<sup>20</sup> The safety and efficacy of a WOCA strategy to prevent UTI in spinal cord injury was described by Salomon.<sup>21</sup> During pregnancy, the risk for UTI associated with asymptomatic bacteriuria increases. It explains the recommendation for screening and treatment of asymptomatic bacteriuria in patients without a neurogenic bladder to prevent pyelonephritis, which can initiate preterm labour and delivery.<sup>22</sup> During pregnancy in SCI women using CIC, the diagnosis and prevention of UTI are hazardous because asymptomatic bacteriuria is frequent. A recent prospective study of six SCI pregnant women under WOCA showed a significant reduction in UTI and antibiotic consumption with no severe adverse events.<sup>6</sup> In our study, a WOCA programme was prescribed in 75% of pregnancies, but with a large heterogeneity at the start of treatment (before or during pregnancy, sometimes late). Patients were included from the time of first medical contact in the NeuroUrology or Infectious Diseases Department, regardless of the pregnancy term. This treatment heterogeneity can explain the absence of relation found between WOCA programme use and urinary infection, unlike a recent retrospective study of 20 pregnancies.<sup>11</sup> A larger-scale prospective study is mandatory to evaluate WOCA efficiency and to propose recommendations for SCI pregnant women.

Few data are available on botulinum toxin use during pregnancy and breastfeeding. Its use is contraindicated during these periods, and for safety a six-month delay was proposed between last injection and beginning of pregnancy. Botulinum toxin injections are planned during the first half of the cycle for women of childbearing age, with beta-HCG assay negative. Despite these precautions, botulinum toxin has been injected in one patient at the very start of pregnancy, when she did not know that she was pregnant. There was no effect on the foetus during pregnancy or during the neonatal period. Literature data on botulinum toxin use during pregnancy are reassuring, without any foetal or neonatal toxicity reported.<sup>23</sup>

Among the five pregnancies with augmentation cystoplasty, all under WOCA, there was one miscarriage and two pyelonephritis with upper tract obstruction requiring double-J ureteric stent for one and some lower UTIs. The pregnancy did not affect the renal function. These results are consistent with those in another study of 20 pregnant women with treated and reconstructed congenital urinary tract abnormalities, including 13 augmentation cystoplasty: 52% UTI and 10% upper tract obstructions.<sup>24</sup> The mechanism proposed to explain upper tract obstruction during pregnancy was the increase in foetal pressure on the less robust neobladder. Interdisciplinary cooperation between urologists and obstetricians was stressed in case of caesarean section for women with augmentation cystoplasty, even if there were no postoperative complications in this study.<sup>24</sup>

A high rate of caesarean section (68%) was realized in this study, with more than half for neurologic reasons, in comparison to the general population (21% in France in 2010)<sup>25</sup> and to the other studies (22–67%).<sup>4,5,8–10</sup> It is well known that vaginal delivery is possible even for paraplegia and tetraplegia patients.<sup>7,26</sup> However, some neurologic cases have discussed the risk of worsening of syringomyelia or urinary stress incontinence by straining during the second stage of labour. Many cases of elective caesarean sections were reported in patients with congenital or post-traumatic syringomyelia,<sup>27–29</sup> which leads to a consensus for caesarean section in the case of syringomyelia.<sup>30</sup> However, a successful operative vaginal delivery without voluntary maternal expulsive efforts in a patient with syringomyelia was documented, without postpartum complication.<sup>31</sup> In our study, all patients with syringomyelia underwent a caesarean section, which explains the high rate of caesarean section. The elective caesarean

section in patients with neurologic sphincter failure to prevent worsening of urinary or faecal incontinence is further discussed. This strategy was reported for other causes of sphincter failure (bladder extrophy),<sup>32</sup> but is not consensual (vaginal delivery is promoted in spina bifida).<sup>33</sup> There is no recommendation for the mode of delivery in cauda equina syndrome; further work is required.

Anaesthesia was induced during labour in all patients with spinal injury at or above T6, mainly by means of epidural catheter, which was maintained for 24–48 h postpartum to prevent autonomic dysreflexia. Despite these precautions, one patient suffered a frontal brain haematoma, with a good neurologic outcome. Current recommendations promote epidural anaesthesia, early in labour and prolonged 24–48 h postpartum, to prevent and treat autonomic dysreflexia.<sup>26,34,35</sup> The optimum dosage and duration of drugs administered by means of a epidural catheter are still under discussion. Some authors suggest placing the epidural catheter two or three weeks before the date of predicted childbirth,<sup>36</sup> but others do not recommend it because of the risk of infection or catheter displacement.<sup>34</sup> Several measures associated could also prevent autonomic dysreflexia (limited pelvic floor examination, avoiding speculum and prevention of bladder distension). Labour, delivery and postpartum are particularly potent stimuli to the development of autonomic dysreflexia, even for people with no previous history of autonomic dysreflexia.<sup>35</sup> High SCI women should be referred for anaesthesia consultation early during pregnancy to prepare an appropriate plan for labour management. Anaesthetists, obstetricians, midwife and nurses who will take care of these patients should be trained in autonomic dysreflexia issues.

## CONCLUSION

This observational study reports a consecutive series of 37 pregnancies in 25 SCI patients. Despite some complications as in previous studies, mothers' and infants' outcomes were satisfying: low prematurity rate and no neonatal complication except for twin pregnancy born at 33 weeks. Pregnancy in SCI women requires many adjustments (adaptation of neurogenic bladder management, prevention of autonomic dysreflexia by prolonged epidural anaesthesia and choice of the mode of delivery). Pregnancy must be prepared by a preconceptional consultation, and managed by a multidisciplinary team involving specialists of neurological disability and pregnancy to provide the best care for mothers and infants.

## DATA ARCHIVING

There were no data to deposit.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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