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Pregnancy experience in women with spinal muscular atrophy: a case series

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Many women with spinal muscular atrophy (SMA) types II, III, and IV reach fertile age, and some of them may consider pregnancy. However, limited data are available about the potential effects of pregnancy on the course of SMA and the outcomes of pregnancies in these patients. Furthermore, the use of several disease-modifying therapies for the treatment of all types of SMA is expected to increase the number of female SMA patients considering pregnancy in the coming years. The aim of this report is to provide clinicians with an overview of the patients in our cohort who have experienced pregnancies.

We conducted a retrospective analysis on these women, through the administration of a questionnaire, which investigated how they experienced the different stages of the pregnancy. Ten patients (3 SMAII; 7 SMA III) participated in the survey; 40% had pregnancies for a total of nine, six of which were term-pregnancies. The mean age of first pregnancy was 32.5 ± 7.8 years for SMA II patients, and 30.5 ± 2.1 years for SMA III. All pregnancies ended in cesarean sections. Interestingly, the *sitters had* more frequent complications in pre-term labor and delivery, but the newborns were all healthy.

This report shows that a successful pregnancy is possible in female patients with SMA. However, the ideal approach should involve a standardized multidisciplinary team capable of effectively addressing every possible scenario. For this reason, it is critically important that clinicians working with SMA patients gain more in-dept knowledge about this topic.

Key words: SMA, pregnancy, outcomes, motherhood, multidisciplinary

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Introduction

Spinal muscular atrophy (SMA) is a genetic disorder usually associated with a defect in the survival motor neuron-1 (SMN-1) gene, which is located in 5q11.2-q13.3. It is characterized by the progressive degeneration of anterior horn neurons in the spinal cord and brainstem nuclei, resulting in progressive muscular atrophy, muscle weakness, and muscle paralysis [1]. Impairment of motor function, muscle weakness and progressive disability are characteristic of all SMA phenotypes, although age at onset of significant motor function loss varies considerably between the different groups [2]. SMA is typically classified into four phenotype based on the age of onset and maximum motor function milestone achieved: 1.SMA type I has onset in the first month of life, with a disability to sit unsupported and needing breathing support, with a survival chance of only up to 2-years old; 2.SMA type II has onset between 6 and 18-months old, with the best motor ability to sit alone without support;3. SMA type III has onset between 18 months and 30-years old, with the ability to stand and walk without support; and 4. SMA type IV has adulthood onset and tends to have normal mobility with mild muscle weakness [3]. Although the clinical manifestations of SMA are now considered to belong to a single spectrum without clear delineation of subtypes, the classification remains useful for clinical purposes. However, the natural his-

tory of the disease is drastically changing with the therapies currently available [4].

Anyway, many women with SMA type II, III and IV reach adulthood with a clinical picture, which may range from minimal motor impairment to almost complete loss of motor skills, and some of them may consider pregnancy. We should consider that many patients with SMA Type III are ambulatory during pregnancy, while the totality of women with Type II are wheelchair-bound. Little data are available of pregnancy effects on the SMA course and about the outcomes of pregnancies in SMA women and their newborns [5]. The aim of the study was to describe our experience and focus on motherhood in patients with SMA for the next future.

Methods

We conducted a retrospective analysis on the cohort of women with SMA followed at the Department of Neurosciences of Federico II Naples University, by giving them a questionnaire made up of 23 items which investigated several aspects concerning their experience on the pregnancy (Appendix 1), with a special focus on maternal and fetal complications, prematurity, mode of delivery, anaesthesiologic risk, respiratory function, breastfeeding and influence of pregnancy on the course of the disease.

Results

Our cohort included 10 females with SMA, seven of which with SMA III and three with SMA II. None had medical assisted procreation. All have done genetic counseling, one of which was pre-conception (Tab. I). All had scoliosis, one surgery (Tab. II). No one was in therapy, at the beginning of the pregnancy.

They had a total of nine pregnancies, six of which were term-pregnancies, two miscarriages and one voluntary interruption of pregnancy. The pregnancies occurred between 1993 and 2021. The middle age of first pregnancy was 32.5 ± 7.8 years for SMA II patients, and 30.5 ± 2.1 years for SMA III. Two patients with SMA III referred worsening of motor symptoms after delivery (confirmed with the Hammersmith Functional Motor Scale - HFMS) and chronic back pain during pregnancy. All maintained a stable respiratory function (Tab. II).

Two SMA II patients had two pregnancies each, all resulting in preterm labor. Two patients with SMA III had one pregnancy each, resulting in full-term labor. All pregnancies resulted in caesarian delivery performed under epidural anesthesia, except one under general anesthesia. Three were emergency caesarian sections.

One patient with SMA II had pneumonia after delivery requiring hospitalization and cough machine use. In three cases, all SMA II mothers, birth complications such as cardiorespiratory arrest, respiratory insufficiency and toxic megacolon occurred. Newborn outcomes were all healthy (Tab. III). Only two patients breastfed, but they early interrupted.

Table I. Pregnancies in our cohort of female patients with SMA.

	SMA III	SMA II
Numbers of female patients	**7**	**3**
Ambulant subjects	4	0
Total number of pregnancies	**2**	**7**
Full-term pregnancies	2 (100%)	0
Pre-term pregnancies	0	4 (57%)
Medically assisted procreation (MAP)	0	0
Genetic counseling Pre-conception counseling Pre-natal counseling	2 (100%) 0 2 (100%)	4 (100%) 1 (25%) 2 (50%)
Abortion	0	2 (29%)
Voluntary interruption of pregnancy	0	1 (14%)

Discussion

Historically, the presence of a neuromuscular disorder (NMD) has been considered a contraindication for pregnancy. Weakness of abdominal wall muscles, impaired respiratory function and vital capacity, the hazards associated with general anesthesia, and, most importantly, the lack of procedural guidelines discouraged both physicians and patients. However, as medical knowledge advances, reports of successful pregnancies in women with SMA or other NMDs have increased, thereby inspiring other patients to pursue motherhood [5-10]. For this reason, it is critically important that clinicians working with SMA patients gain more in-dept knowledge about this topic, and ultimately be prepared to guide their patients through such a crucial decision. Our experience shows that a successful pregnancy is possible in SMA.

Women with SMA generally had good outcomes and have chosen to have more than one pregnancy [7,8]. They report experiencing pregnancy feeling stronger and satisfied. Of note, sitters more frequently experienced complication in labor and pre-term births. On the other hand, all SMA patients, even if not wheelchair-bound, had a caesarian section (Tab. IV). It is therefore worth making some considerations. Vaginal delivery is not contra-indicated, as uterus is autonomically innervated,

Table II. Cohort characteristics of female patients with SMA who had pregnancies.

Patient ID	SMA type	Age at pregnancy	Max motor function	Last motor function	Scoliosis	Scoliosis surgery	Ventilation
#1	II	38	Sitter	Sitter	+	-	-
#1	II	42	Sitter	Sitter	+	-	-
#2	II	27	Sitter	Sitter	+	-	-
#2	II	30	Sitter	Sitter	+	-	-
#3	III	32	Ambulant	Ambulant	+	-	-
#4	III	29	Ambulant	Ambulant	+	+	-

Table III. Pregnancy outcomes in our cohort of women with SMA.

Patient ID	SMA type	Age at pregnancy	Preterm labor	Cesarian section delivery	Anesthetic management	Respiratory function	Worsening of motor symptoms	Birth complications	Newborn outcomes	Other complications
#1	II	38	+ (34 w)	+ (elective)	Epidural anesthesia	Stable	-	Cardiorespiratory arrest (CPR)	Healthy	Chronic back pain
#1	II	42	+ (35w+5d)	+ (emergency)	Epidural anesthesia	Stable	-	-	Healthy	Post-op weakness (1° week)
#2	II	27	+ (34w)	+ (elective)	Epidural anesthesia (difficulty in LP)	Stable	-	Respiratory distress (ETI)	Healthy	Gestational diabetes Post-op weakness (1° week)
#2	II	30	+ (34w)	+ (emergency)	Epidural anesthesia	Stable	-	Toxic megacolon (surgery)	Healthy	Pneumonia (cough assist machine) Dysphagia
#3	III	32	-	+ (emergency)	Epidural anesthesia	Stable	+ (after delivery)	-	Healthy	Post-op weakness (1° week)
#4	III	29	-	+ (elective)	General anesthesia	Stable	+ (after delivery)	-	Healthy	Chronic back pain

Table IV. Cohort pregnancy comparative results.

	SMA II	SMA III
Full-term pregnancy	0 *	2 (100%)
Preterm labor	4 (57%)*	0
Cesarian section delivery	4 (100%)	2 (100%)
Breastfeeding	1 (25%)	1 (50%)
Motor weakness worsening after delivery	0	2 (100%)
Birth complications	3 (75%)	0

*3/7 Abortion or Voluntary interruption of pregnancy (see Tab. I).

and should not be affected by the disease. However, marked weakness of abdominal muscles could limit the ability of severely affected women to push effectively during labor, and some cases of ineffective contractions and respiratory failure during contractions have been reported, related to the increasing prevalence of scoliosis and decreased pulmonary function in non-ambulatory women. Therefore, the health care providers should be prepared to perform caesarian sections if necessary[11--13]. Furthermore, especially in women confined to wheelchair, pelvis may be distorted because of the disease and pelvic diameters may be reduced, so that in some cases the positioning of the patient on the operating table and the access to the uterus may be difficult, even due to the fixed contractures in the legs [8-10].

Female patients with SMA may experience worsening of their baseline motor function during pregnancy, which may or may not regress after delivery; 31% to 42% women reported an exacerbation of weakness during pregnancy [5]. In our cohort (Tab. IV), the ambulant patients refer a greater worsening of motor function, stabilized in the course of the disease, after delivery. The reason of this worsening is unclear. Therefore, assessment of functional status before conception and a regular monitoring during pregnancy and in the post-partum period are recommended [6].

None of our patients was been treated with nusinersen or risdiplam at the time of pregnancy because the pregnancies preceded the therapies currently available, except in one case who chose to start nusinersen four months after giving birth, interrupting breastfeeding.

Conclusions

The management of pregnancy and delivery in female patients with SMA requires a careful balance between fetal and maternal needs, including considerations such as the timing of labor, the possibility of instrumental or operative delivery, anaesthesiologic risk assessment, respiratory function management, fatigue, back pain, and breastfeeding. An appropriate approach should involve a standardized multidisciplinary team including medical specialists in obstetrics, neurology, neonatology, clinical genetics, anesthesiology, pulmonology, and trained nurses. This team should also provide postpartum care and supporting during breastfeeding. Unfortunately, this ideal team is not yet readily available, perhaps because pregnancy has not been adequately addressed in the care of women with SMA.

Furthermore, we have limited knowledge about the risks to fetal development associated with the therapies currently available and their safety during breastfeeding.

This report highlights the importance of considering the motherhood experience in the management of female patients with SMA. Last but not least, the inclusion of the current disease-modifying therapies into this comprehensive approach in the near future should be encouraged.

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Conflict of interest statement

The authors declare no conflict of interest.

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Authors' contributions

RPB: performed acquisition and analysis of data, revision of the literature and drafting of the manuscript; DZ, AR and EC: acquisition of clinical data; ST, RI, RD, FM and LR: revision of the manuscript.

Ethical consideration

The disclosure of this retrospective study was approved by patients via informed consent. The study was approved by the Ethical Committee at the "Federico II University-AORN A. Cardarelli" (project number 15184/2023).

NOTE. This study was accepted and presented as *oral communication* at the 23rd Congress of the Italian Association of Myology, held in Padua from 8 to 10 June 2023

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Appendix 1. Questionnaire submitted to SMA female patients.

1. Have you had any pregnancy?
2. If yes, how many pregnancies have you had?
3. Have you had any spontaneous abortion? If yes, at what week?
4. Did you voluntary terminate the pregnancy?
5. Have you made genetic counseling? Which type (pre-natalpre-conception)?
6. Did you undergo medical assisted pregnancy?
7. How old were you when you had your first pregnancy? and how many in the others?
8. Have you had full-term or pre-term pregnancy?
9. If pre-term, what week did you give birth? and for what problem?
10. What was your motor function at the time of each pregnancy? Were you ambulant or in a wheelchair?
11. How did you feel during the pregnancy, specifying during each trimester? (strong, weak, enthusiastic, tired, other)
12. What was your level of fatigue on a scale from one to ten? Has it increased due to weight gain?
13. Did you have any respiratory complication during pregnancy?
14. Did you need any kind of ventilation?
15. Have you had musculoskeletal pain?
16. Did you have vaginal or cesarean delivery?
17. Was it an elective or emergency cesarean section?
18. If emergency, for what problem?
19. What type of anesthesia did you undergo? Have you had any complication?
20. Were there any complications for the newborn during and after delivery? What kind?
21. How did you feel after delivery? What was your level of fatigue?
22. What was the outcome of the newborns?
23. How would you describe the pregnancy experience?