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Highlights

- In pregnancy of patients with MS gestational weeks and birth weight were lower compared with HS
- Caesarean section rate was increased in women who received the diagnosis before pregnancy
- We observed an increase of both planned and urgency caesarean sections

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Cesarean section in women with MS: a choice or a need?

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Abstract.

A multidisciplinary approach is needed for the management of pregnancy related issues in women affected by Multiple Sclerosis, however little attention has been devoted to the modality of delivery. Here we aimed to investigate whether the diagnosis of multiple sclerosis (MS) influences delivery modality in MS patients. Patients who received the diagnosis before pregnancy showed a lower frequency of natural delivery and a higher frequency of both planned and urgency caesarean sections. Gestational weeks and birth weight were lower in MS patients when compared with healthy subjects. The diagnosis of MS may drive the decision of the gynaecologist to perform a caesarean delivery.

Dear Editors,

A multidisciplinary approach is needed for the management of pregnancy related issues in women affected by Multiple Sclerosis (MS) [1]. Several aspects related to pregnancy have been widely investigated in MS, however little attention has been devoted to the modality of delivery. There is evidence that MS patients have greater need for instrumental delivery than the general population [2]. On the other hand, Caesarean delivery (CD) is not associated with adverse effects on delivery or the postpartum MS course [3]. Compared to healthy women, MS patients are not at higher risk for pregnancy complications such as spontaneous abortions (SA), placental abnormalities, ectopic pregnancy, antepartum hemorrhages, preeclampsia, stillbirth and preterm births [3]. Babies born to mothers with MS are often found to be smaller, [4] but other studies show birthweights to be equal to the general population [5].

The main objective of the present analysis was to investigate whether the diagnosis of MS influences delivery modality and to confirm whether gestational weeks and birth weight were lower in MS patients compared with HS.

We performed an observational retrospective study. At MS centre of Sant' Andrea Hospital in Rome, from November 1, 2017 to August 31, 2018, we administered a questionnaire on pregnancy to a consecutive cohort of patients with fully ambulatory MS. An Obstetrician was responsible for the distribution of questionnaires. All MS subjects signed informed consent and were asked to fill out a self-administered, anonymous questionnaire, exploring pregnancy issues. Questionnaires included data on pregnancy outcome (term delivery, elective termination), birth weight, delivery methods (elective or emergency CD) and obstetric complications. We also collected data on healthy subjects (HS) to be used as controls. Data were collected from clinical registry of Fabia Mater clinic in Rome. Patients with incomplete pregnancy histories were excluded from the analyses.

Differences between HS and MS patients in the pregnancy outcome and delivery modality were tested with unpaired t-test for continuous variables and chi-square test for categorical variables by means of SPSS Statistics.

We collected data on pregnancy from 250 HS and 157 MS patients (mean age 33 ± 5.8 vs 30 ± 5.8 , $p < 0.001$ by unpaired t-test). In patients with MS, gestational weeks and birth weight were lower compared with HS (38.4 ± 1.7 vs 39.3 ± 1.3 weeks $p = 0.001$ and 3092 ± 519 vs 3290 ± 446 g $p < 0.001$ respectively). In 76 patients the diagnosis of MS preceded the pregnancy (MSpre), 81 received the diagnosis after pregnancy (MSpost), eleven of them had experienced a neurological symptom before the pregnancy. Table 1 summarises the demographic characteristics and pregnancy outcome according to study group. Compared with HS, the MSpre group but not the MSpost showed a lower frequency of natural delivery and a higher frequency of both planned and urgency caesarean section (CS) (39.3% vs 66% ; 32.7% vs 22.4% and 24.5% vs 9.2% respectively, $p < 0.001$). Birth weight was lower in both MSpre and MSpost when compared with HS.

We observed that women with a diagnosis of MS are more subject to CS and with an increase of both planned and urgency CS. We suggest that an aprioristic choice of the gynaecologist may account for this difference. Several factors may explain the increase of urgency CS in MS population. Unfortunately, the risk of obstetric complication in MS patients has been assessed in few studies [2;4;6]. Some reports suggest that birth process may be affected in MS [7] and that MS-related symptoms such as neuromuscular perineal weakness, spasticity, fatigue and exhaustion, could be important factors for failure in the late phases of labour that should be evaluated in each case [7]. Unfortunately, data specifically regarding those issues are not available in our study. The high incidence of planned CS suggests that gynaecologist perceived MS “per se” as a risk for women and offspring higher than risks related to the surgical intervention. This is of particular relevance considering that CS increases the risk of maternal mortality and maternal morbidity including uterine rupture, abnormal placentation, ectopic pregnancy, stillbirth, and preterm birth [8]. Furthermore CS may subtly alter neonatal physiology through the exposure to different hormonal, physical, bacterial, and medical environment [8]. Nevertheless, some benefits of CS, such as less frequent incontinence and urogenital prolapse have been described [8]; this could be an aspect to consider for MS with severe bowel/bladder symptoms. Of particular relevance, we found a lower gestational age and a lower birth weight in all sample of patients with MS. Some authors discuss a reduced (but still in the normal range) birth weight for newborns of mothers with MS, compared to healthy controls [4-9]. Our data support this observations. We found those results in all MS patients suggesting that they are related to maternal and foetal factors rather than to obstetricians concerns about MS. However, we could speculate that a lower gestational age, usually related with CS, could have affected this data. Our study did not highlight other medical issues related to low gestational age and a low birth weight. However, as a limit of the present study, we collected data of MS patients through a questionnaire, therefore we can not exclude that a recall bias can have affected the completeness of data. Chen et al reported also that a significantly higher proportion of urinary tract infections among MS mothers, compared with HS, suggesting that

suboptimal intrauterine conditions and fetal growth might result from neuronal dysfunction in pelvic organs [7]. Finally, exposure to disease-modifying therapy (DMT) during early pregnancy in women with MS is increased with an increasing number of pregnancies conceived on DMT over the more recent years [1;10]. Interferon β exposure has been associated with both lower baby weight and length [1;10]. Thus, the recent use of DMT may have significant impact on newborns' somatometric features.

We suggest that a tighter communication between neurology and gynaecology practitioners could improve patients' management and promote an individual-based choice; prospective studies assessing the obstetric risks in relation with clinical characteristics are needed.

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Table 1. Delivery modality and pregnancy outcome according to study group. Data are expressed as mean (SD) or number (%) as appropriate;

	HS	MSpre N=61	MSpost N=78
Age, years	33.0 (5.8)	33.6 (5.1)	28.2 (5.05)*
Natural	165 (66%)	24 (39.3%)*	50 (64.1%)
Operative	7 (2.8%)	2 (3.2%)	1 (1.2%)
Planned Cesarean section	56 (22.4%)	20 (32.7%)*	17 (21.8%)
Urgency Cesarean section	23 (9.2%)	15 (24.5%)*	10 (12.8%)
Gestational age, weeks	39,3 (1.3)	38.4 (1.61)*	39.1 (1.65)
Birth weight, g	3290 (446)	3002,1 (539)*	3162 (494) [§]

p values refer to chi square test using HS as reference group * $p < 0.001$, § $p < 0.05$.

Conflict of Interest

SF, CDA have nothing to disclose; LDG received speaking onoraria from Genzyme and Novartis, travel grant from Biogen, Merk, Teva, consulting fee from Genzyme, Merk and Novartis; SR received fee as speaking honoraria from Teva, Merck Serono, Biogen, travel grant from Biogen, Merck Serono, fee as advisory board consultant from Merck Serono and Novartis; GB received consulting and lecture fees and travel grants from Almirall, Bayer, Biogen, Genzyme, Merck Serono, Novartis, Roche and Teva; CP received consulting and lecture fees and research funding and travel grants from Almirall, Bayer, Biogen, Genzyme, Merck Serono, Novartis, Roche and

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