

Reciprocal Effects of Multiple Sclerosis, Childbirth, and Postpartum

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ABSTRACT

Background: Multiple sclerosis (MS) is a chronic disease of the central nervous system, which is more prevalent in women than men. Considering the onset of MS in the women of reproductive age, the present study aimed to investigate the reciprocal effects of MS, childbirth, and postpartum.

Methods: This retrospective, descriptive-analytical study was conducted on 110 women diagnosed with MS during pregnancy in Isfahan, Iran during 2016-2017. The subjects had become pregnant within the recent decade and were selected via random sampling. Data on the demographic characteristics, pregnancy and postpartum profile, medicinal changes, symptoms, severity, and attack rates of MS were collected. Data analysis was performed in SPSS version 16.

Results: Mean age at the completion of pregnancy was 38.13 weeks. In total, 63.9% of the deliveries were accomplished via caesarean and 35.1% of the women had natural vaginal delivery. Mean pain intensity at childbirth was 7.11. No symptoms of MS attacks were reported in 86.7% of the subjects during delivery and 90.7% of the women within the first six weeks of childbirth. All the neonates were healthy, and 66.3% of the mothers had no psychological and emotional postpartum complications. In addition, 40.3% of the women started their MS medication within the first six months after childbirth.

Conclusion: According to the results, MS was not associated with the increased risk of preterm or post-term delivery. Moreover, it did not increase the severity of labor pain in the mothers. On the other hand, the rate of elective cesarean section was higher in MS patients compared to the general population, especially in the cases with disabilities. According to the Friedman curve, MS caused no substantial changes in the progression of delivery, and most of the neonates were healthy males with an Apgar score of 10. However, the severity of limb numbness and blurred vision increased in the women with MS in the postpartum period.

Keywords: Childbirth, Multiple sclerosis, Postpartum, Pregnancy

Introduction

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system (CNS), which has an autoimmune origin (1). MS is a chronic, multifactorial disease caused by a combination of environmental and genetic factors (2). Recently, the prevalence of MS has been reported to be on the rise. According to the World Health Organization (WHO), more than two million people suffer from MS across the world (3). Furthermore, statistics suggest that in 2013, approximately 2.3 million people were affected by MS (4).

A study has denoted that the prevalence of MS is medium to high in Iran (5). Additionally, the findings of Valiani et al. and Tolou-Ghamari et al.

have indicated that Isfahan province has the highest prevalence rate of MS in Iran (6.7). The prevalence of MS is twice higher in women than men (8), with the rate gradually increasing in women (6.9). The majority of MS patients experience the onset of the symptoms in the second and third decade of their life (10). Therefore, MS is most commonly diagnosed in the women of reproductive age (11).

Pregnancy suppresses the autoimmune activities of many cells; as a result, pregnancy will cause stopping diseases such as rheumatoid arthritis and even MS as an inflammatory disease of the CNS. According to a research, the recurrence of MS reduces by 80% during

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Please cite this paper as:

Valiani M, Ashtari F, Mokhtari F. Reciprocal Effects of Multiple Sclerosis, Childbirth, and Postpartum. Iranian Journal of Neonatology. 2018 Sep; 9(3). DOI: [10.22038/ijn.2018.28749.1384](https://doi.org/10.22038/ijn.2018.28749.1384)

pregnancy, particularly in the third trimester (12), while the disease may be exacerbated in the patients during the postpartum period as opposed to before pregnancy (11). On the other hand, Karp et al. claimed that the rate of relapse in a group of pregnant women with MS was lower compared to non-pregnant women within the first years after pregnancy (10).

The frequency of MS attacks during and prior to pregnancy is an important predictor of the risk of recurrent attacks in the postpartum period (13). The results of the mentioned study also showed that the rate of recurrent visual symptoms of MS was significantly higher within the first year after childbirth, especially in the first 3-6 months postpartum (14). Although no studies have investigated the role of exclusive breastfeeding, vitamin D deficiency, stress, and dietary patterns on the severity of MS in pregnant women, some findings have denoted that the risk of MS recurrence is lower by half in the women who breastfed their infants compared to those who did not engage in breastfeeding (15).

Considering the high incidence rate of MS in women (especially those of reproductive age), fear of the impact of the disease on delivery stages and infants' health, onset and exacerbation of the symptoms in the postpartum period, breastfeeding, and neonatal care, MS is associated with numerous challenges for the women of reproductive age. The present study aimed to investigate the reciprocal effects of MS, childbirth, postpartum, and neonatal health.

Methods

This retrospective, descriptive-analytical study was conducted on 110 women diagnosed with MS with a history of pregnancy in Isfahan, Iran during 2016-2017. The files of the patients were available in the treatment deputy of the hospital. Women with MS who had become pregnant during the recent decade were selected via census sampling. The contact numbers of the patients were retrieved from their medical records; the selected subjects were contacted, and after obtaining informed consent, data collection checklists were completed by the researcher via phone.

The checklist had three sections; the first section consisted of demographic data, and the second section contained the pregnancy profile, including the type of pregnancy, duration of labor phases, labor pain intensity (based on the visual analogue scale). The third section of the checklist was about the postpartum phase, including data on the severity of hemorrhage,

length of hospital stay, Apgar score, health status, and gender of the neonate, dietary pattern of the neonate, length of breastfeeding, medication use after childbirth, MS symptoms after childbirth, emotional complications, medicinal changes, and the symptoms, severity, and attacks of MS.

Data analysis was performed in SPSS version 16 using t-test, Chi-square, and analysis of variance (ANOVA).

Ethical Considerations

After inviting the participants to enroll in the study, the research objectives and procedures were fully explained, and informed consent was obtained from all the subjects.

Results

In total, 110 women with MS with the mean age of 32.4 years were enrolled in the study. In terms of occupation status, 88.2% of the women were housewives, 8.2% were employees, and 3.6% were self-employed. The majority of the participants had a high school diploma or below (53.6%), and 46.4% were had academic education.

The economic status of the family was medium in 73.6% of the women, unfavorable in 10%, favorable in 9.1%, and poor in 7.2% of the subjects. Disease type was primarily progressive in 8.7%, secondary progressive in 6.5%, recurring and diminishing in 81.5%, and progressive relapsing in 3.3%. None of the patients had acute or malignant MS. The frequency of MS attacks in the patients is presented in Table 1.

Mean age at the completion of pregnancy was 38.13 weeks. Regarding the mode of delivery, 63.9% of the women had caesarean section, 32% had natural vaginal delivery, and 3.1% had assisted natural delivery. Among the subjects with natural delivery, 52.2% had spontaneous onset of pain, and 47.8% received oxytocin induction.

Based on the visual analogue scale (VAS), the severity of labor pain was 7.11 in the studied women. Pain intensity was 1-3 in 11.4% of the mothers, 4-6 in 25.7%, and 7-10 in 68.8% of the women. Duration of labor phases is shown in Table 2.

Within an hour after delivery, the majority of the subjects had moderate bleeding (59.8%), while 13.0% had substantial hemorrhage, 12.0% had high hemorrhage, 7.6% had low hemorrhage, and 7.6% had very low hemorrhage. Mean length of hospital stay was 1.26 days. The majority of the women (76%) were hospitalized for one day, 21.9% for two days, and only 2.1% were

Table 1. Frequency of Multiple Sclerosis (MS) Attacks One Year before Pregnancy, during Pregnancy, and after Childbirth

Frequency of Attacks	Time				
	One Year before Pregnancy (%)	During Pregnancy (%)	After Childbirth		
			First Six Weeks Postpartum (%)	Three Months Postpartum (%)	One Year Postpartum (%)
None	69.2	86.2	90.7	86.9	81.8
1	25.2	10.1	7.2	9.1	10.1
2	2.8	2.8	1.0	1.0	6.1
3	1.9	0.9	0.0	3.0	1.0
4-10	0.9	0.0	1.0	0.0	1.0

Table 2. Duration of First, Second, and Third Labor Phases in Women with MS

Variable	Duration	Frequency	Percentage	Total
1 st Phase of Labor (hour)	1-3	14	43.8	100 (110)
	4-8	16	50.1	
	≤9	2	6.2	
2 nd Phase of Labor (minute)	15≥	6	21.4	100 (110)
	16-30	19	67.9	
	31-60	3	10.7	
3 rd Phase of Labor (minute)	5≥	14	50.0	100 (110)
	6-15	11	42.3	
	16-30	2	7.6	

Table 3. Frequency of Postpartum Psychological and Emotional Complications in MS Patients

Type	Frequency	Percentage	Total
Postpartum Blues	19	65.5	100 (32)
Postpartum Depression	9	32.1	
Postpartum Psychosis	1	3.4	

Table 4. Start Time of MS Medication in Mothers after Childbirth

Time	Frequency	Percentage	Total
First Six Months Postpartum (0-6 Months)	29	26.4	100 (110)
Second Six Months Postpartum (7-12 Months)	13	11.7	
Third Six Months Postpartum (13-18 Months)	14	12.6	
Fourth Six Months Postpartum (19-24 months)	5	4.5	
After 24 Months	11	9.9	
No Visitation to Receive Medication	38	34.5	

hospitalized for three days.

In this study, 55.7% of the newborns were male, and 44.3% were female. One-minute Apgar score of the neonates was nine in 98.9% and eight in only 1.1% of the neonates. The five-minute Apgar score was 10 in 97.9% of the infants and nine in 2.1%. In addition, 59.8% of the infants were breastfed, 16.5% were fed with formula, and 23.7% were fed with the combination of breast milk and formula. In terms of the duration of breastfeeding, 33% of mothers breastfed for six months, 17.6% breastfed for 7-12 months, 22% breastfed for 13-18 months, and 27.5% breastfed for 19-24 months after childbirth and continued breastfeeding.

Among the participants, 27.4% needed help for infant care, while 45.3% did not need help, and 27.4% needed some help. Some of these women (76.8%) were supported by their spouses during pregnancy and after childbirth, while 9.5% received no support, and 13.7% had some support from their spouses. In the present study, 76.3% of

the mothers had no psychological complications after childbirth. Psychological and emotional issues after childbirth were observed in 33.7% (n=32) of the participants (Table 3).

In 40.3% of the women, MS medication initiated within the first six months postpartum. The starting time of MS medication after childbirth is shown in Table 4. The most frequently consumed MS medications by the subjects were Sinovex (40.9%), Resigen (20.5%), Betaseron (11.4%), Osvimer (9.1%), Rebif (6.8%), Avonex (4.5%), and intravenous immunoglobulin (2.3%).

The first postpartum MS attack was reported in the first six weeks after birth in 30% of the subjects, within seventh week to the third month in 15%, and within the third month to one year postpartum in 55% (Table 1). According to the self-report of the patients regarding the symptoms of MS, 54.5% of the women had numbness, 19.7% had blurred vision, 4.5% had other symptoms, and symptoms such as weakness, fatigue, tremor, and

urinary symptoms were reported in 3%. Moreover, symptoms such as muscle stiffness and spasms, digestive problem, dizziness, speech problems, and memory and mood problems were intensified in 1.5% of the studied subjects.

Discussion

Pregnancy and childbirth are natural processes in a woman's life. MS mostly appears in the young women of reproductive age and is one of the most common causes of neural disability in the youth (3). In the present study, the mean age of the subjects was 32.4 years, and the majority of the women had the recurring and diminishing MS. According to the literature, the average number of the children born to women with MS is lower than the general population in a specific region (16). Therefore, this disease challenges women with the impact of the disease on labor process, baby's health as well as the impact of childbirth and breastfeeding on the course of disease.

According to the results of the present study, the majority of the women gave birth in the due course. Mean age at pregnancy completion was 38.13 weeks; therefore, MS was not associated with the increased risk of preterm or post-term delivery. While MS is not a contraindication for natural delivery, our findings indicated that 63.9% of the women preferred caesarean section. In general, statistics suggest the noticeably high rate of caesarean section in Iran, and our patients were not an exception in this regard. However, the results of some studies, which are in line with the current research, have shown the rate of elective caesarean section to be higher in the women with MS; it could be inferred that MS influences the decision of women regarding the mode of delivery (17, 18). In a study, Ferraro et al. denoted that MS had no substantial effect on the rate of cesarean section (16). In general, the studies in this regard have not confirmed the increased risk of obstetric complications in the women with MS compared to the normal population. Although there are conflicting results in this respect (19), the rate of elective cesarean section in the women with MS is particularly higher in those with disabilities compared to the general population (17, 18). This could be due to the concerns about neuromuscular disorders, weakness, and spasms in the areas involved in labor (20). In the present study, 36% of the women selected natural vaginal delivery.

In 52.2% of the mothers, the onset of pain was spontaneous. Seemingly, MS did not increase the

need for labor induction. Mean pain severity was 7.11 based on the VAS. Therefore, it could be concluded that MS did not increase the labor pain index in the women, which could help healthcare providers to promote natural delivery in MS patients.

In the current research, the duration of the first labor phase was 4-6 hours in 47% of the women and 1-3 hours in 43.8%, while the duration of the second labor phase was 15-30 minutes in 70% of the mothers. The duration of the first and second phases of labor was justified due to the fact that the majority of the subjects had their first pregnancy. In 50% of the women, the duration of the third phase of labor was less than five minutes.

In the present study, approximately 60% of the women with MS had moderate bleeding after childbirth. Mean length of hospital stay in these women was 1.26 days. Therefore, MS caused no substantial changes in the progression of delivery in accordance with the Friedman curve relative to the general population. Moreover, the length of hospital stay and severity of bleeding in the mothers with MS had no differences with the general population. In this regard, our findings and the study by Lu et al. (2013) indicated that MS is not associated with the increased risk of gynecological and obstetric complications in the patients (21).

Previous studies have not confirmed the increased risk of neonatal complications in the women with MS compared to the general population (17). In the present study, the majority of the neonates were healthy males. More than 97% of the newborns had one- and five-minute Apgar scores of 10. Moreover, 60% of the mothers fed their children exclusively with breast milk, while only 27.5% continued breastfeeding until the end of the second year postpartum.

On the other hand, the results of a similar study indicated that prolonged breastfeeding could reduce the risk of metabolic syndrome in the patients with gestational diabetes and those without the disease (22). In addition, women with gestational diabetes could probably experience stable, long-lasting protective effects on MS analogs (13). Some studies have denoted that the risk of the recurrence of MS symptoms is lower by half in breastfeeding women compared to those with no breastfeeding (10). The results of another study indicated that prolonged breastfeeding (more than four months) exerts protective effects against MS (23). Exclusive breastfeeding has anti-inflammatory and protective effects due to

delayed menstruation recurrence, while feeding of neonates with the combination of breast milk and formula, which expedites menstruation, does not have anti-inflammatory effects (24). Therefore, in addition to the inherent benefits of breastfeeding for infants and mothers, it is a protective factor in the case of the women with poor socioeconomic status. Furthermore, some studies have demonstrated breastfeeding results in protection against asthma, diabetes, and MS in neonates, while its long-term effects remain unknown (23).

The findings of Ragnedda et al. have also indicated that the lack of breastfeeding or breastfeeding for less than three months is associated with the increased risk of MS in adulthood. However, factors such as the neonate's gender and population of MS patients influence the risk of MS, and reduced duration of breastfeeding increases the risk of MS, particularly in male newborns (2).

In this regard, some studies have denoted that the duration of breastfeeding in the women with MS has increased during recent years (from 7.3 months in 2005 to 8.3 months in 2013). In the present study, no significant difference was observed in the decision-making for breastfeeding between the women with MS (77%) and the control group (81%) (16). A research conducted in Norway and Italy showed the significant, protective role of breastfeeding in relation to male gender. The impact of gender on the protective role of breastfeeding is complex; it may be attributed to the helper T-cell immune responses that are associated with breastfeeding, which may affect the vulnerability of newborns to infections (2). Therefore, considering that the majority of the women in the present study had male neonates and mediocre socioeconomic status, it is recommended that completing the course of exclusive breastfeeding and its protective effects on mothers and infants be particularly emphasized in the related educational interventions.

Pregnancy may variably affect some mental disorders. Psychological stress often increases due to postpartum hemorrhage; consequently, the risk of psychological diseases is relatively higher during this period. On the other hand, other factors, such as the stress caused by a chronic disease, have been associated with a higher possibility of developing psychological diseases. According to statistics, approximately 15% of women suffer from a type of non-psychotic, depressive disorder within six months after childbirth. In more than half of mothers (50-80%),

maternal blues occur after delivery nearly within a week after childbirth (25).

In the present study, 33.7% of the women experienced emotional and psychological complications after childbirth. Among these subjects, 65.5% had maternal blues, 32.1% had major depression, and 3.4% had psychosis. According to the statistics reported by the Center for the Control and Prevention of Diseases, the prevalence of postpartum depression is 10-20% (25). Findings of the current research demonstrated that MS was not associated with the risk of developing postpartum psychological disorders. However, considering that the risk of psychological complications (e.g., psychosis) is 10-15 times higher in women with underlying diseases (25), thorough monitoring of pregnant women with MS in terms of psychological disorders is essential.

The results of the present study showed that the majority of the women were able to take care of their newborns without the need for complete support from others. Additionally, these mothers received optimal support from their spouses during pregnancy and childbirth. The two important predictors of the risk of recurrence of MS attacks after delivery are the frequency of attacks during and before pregnancy (13). In this regard, previous findings have denoted that the postpartum period is associated with the aggravation of the symptoms and recurrence of MS relative to pregnancy and even before pregnancy (11). In the present study, 46.7% of the subjects had MS attacks, and 30% experienced their first attack within the first six weeks after delivery. Similar to the other studies, it seems that pregnancy plays a protective role against MS attacks; however, the frequency of the attacks has been reported to increase after childbirth compared to the year before pregnancy (11). On the other hand, some findings have indicated that the rate of recurring MS attacks is lower in the first years after pregnancy compared to non-pregnant patients. In this respect, the results of the present study showed that although pregnancy decreases the symptoms of MS, the consequences of the disease remain the same for pregnant and non-pregnant women in the long run (~10 years). As such, there is only a slight chance for pregnancy to increase the risk of secondary MS attacks (10).

In the current research, 40.3% of the women started MS medication within the first six months after delivery, and the most commonly consumed medication in the postpartum period were

Sinovex and Resigen. Among the symptoms of MS, the severity of limb numbness and blurred vision increased in the postpartum period. Another study in this regard indicated that pregnancy accelerates the onset of MS symptoms, and the onset of visual symptoms increases within one year after delivery. The risk is significantly higher in the first 3-6 months postpartum (14). Considering that most recurrent MS attacks occur within the first four months after childbirth, it is recommended that MS patients receive MS treatment and medication immediately after childbirth (13). The high frequency of postpartum MS attacks in the present study could be due to the delay in starting medication after childbirth.

According to a research in this regard, consumption of intravenous immunoglobulin after childbirth reduces the risk of symptom reversal to 60% within the first year postpartum, especially in the first three months (11). In the present study, intravenous immunoglobulin was only used by 2.3% of the subjects after childbirth. Therefore, it is advisable that the impact of using this drug on MS recurrence and attacks in the postpartum period be further investigated.

In conclusion, it is recommended that neurologists, gynecologists, and midwives not discourage pregnancy in the women diagnosed with MS at the reproductive age and raise their awareness to pave the way for women to make decisions and act in a timely manner in order to become pregnant in good conditions with the controlled course of the disease and proper medication use.

One of the strengths of the present study was exploring the reciprocal effects of MS, childbirth, and the postpartum. Our findings could lay the groundwork for the education and training of healthcare providers. The main limitation of the study was the reference to the recollections of the mothers for data collection, which might have affected the results.

Conclusion

MS disease is not associated with increased likelihood of pre-term or post-term delivery. It has not created a substantial change in the progression of delivery. In this study most of the babies were healthy males and had an Apgar score of 10. The severity of limb numbness and blurred vision increases in the postpartum period.

Acknowledgments

This study was extracted from a research

project approved by Isfahan University of Medical Sciences, Iran in 2017 (code: 192111). Hereby, we extend our gratitude to the Vice Chancellery of Research at Isfahan University of Medical Sciences for the financial support of this study. We would also like to thank all the patients for assisting us in this research project.

Conflicts of interests

None.

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