

Multiple Sclerosis and to Be Woman

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ABSTRACT

Multiple sclerosis (MS) a disease that is chronic, neurological and inflammatory, involves the white matter of the central nervous system. It is demyelinating and progressive, progresses with remissions, and can cause permanent disability. It is often seen in young adults. MS is two times more common in women than in men. It is similar to many chronic diseases in terms of its general symptoms. It affects the life quality of individuals during the reproductive period. It is quite important to evaluate MS in terms of women's life cycles because the rate of the disease increases in women between the ages of 20 and 40 - the most productive period - and because approximately 70% of MS patients are women. In this review, the natural course of life of women with MS was investigated based on up-to-date guidelines and the literature, including their sexual lives, use of contraceptives, pregnancies, giving birth, postpartum period, breastfeeding, assisted reproductive techniques and menopause periods. It was aimed in this review to take into account especially the period of woman's life when preparing treatment programs for women with MS. It was also aimed to have healthcare professionals and nurses to establish healthcare processes in this direction. In conclusion, results reveal that there are limited numbers of studies on the subject and that there is a need to conduct more extensive studies on the subjects that controversial issues.

Keywords: Multiple sclerosis, period of woman's life, woman.

INTRODUCTION

Multiple sclerosis (MS) is a chronic, progressive and neuroimmune disease with unknown exact cause that develops due to demyelination, neurodegeneration and neuroinflammation in the central nervous system (CNS). It is often seen in women and generally between the ages of 20 and 40, accompanied by attacks. MS symptoms are quite diversified and unpredictable. Its symptoms include spasticity, tremor, muscle weakness, sensory disturbances, cognitive problems, bladder-intestine dysfunction, fatigue and gait disturbances. Moreover, numbness, loss of strength, visual problems, vertigo, pain, emotional changes, depression and sexual dysfunction are commonly seen in MS patients and negatively affect their quality of life, [1-3] These symptoms, which are initially seen only during attacks,

gradually settle and become persistent. They make people's lives difficult in many aspects.

MS ranks first among the diseases that cause neurological disability in young adults independent of trauma. It is among the most common demyelinating diseases, affecting 2.3 million people around the world. [4,5] The prevalence and incidence of MS in the world are reported to be 126 in 100 thousand patients and 6.5 in 100 thousand patients, respectively. [6] It was found in a study that the incidence of the disease was 1.74 in 100 thousand people, and the female to male ratio was 2/3. [7] It is more common in whites, in light-skinned people, in those who have a family member with MS, in those who live in mild and cold climate zones, and in those with high sociocultural and economic levels. The

emergence of the first clinical symptom usually corresponds to the age range of 20 to 40. It is quite uncommon for MS to occur at an age as early as two years or as late as the eighth decade. [8]

MS is more common in females than in males. It does not only affect people physically; it also causes serious problems in their family lives, social relations and professional lives. [9,10]

In this review, an attempt was made to draw attention to the effects of MS on women's health.

MS & SEXUAL LIFE OF A WOMAN

As is known, sexual expression and behavior are inseparable parts of human life. Sexuality gives humans the impression that they are worth loving. For a person, any problem related to sexuality is extremely private and difficult to share. Sexual dysfunction in MS is an important health problem, which is quite common but is usually overlooked. [11]

Sexual dysfunction in MS may appear in three forms: primary, secondary and tertiary. [11] The dysfunctions stemming from the damage MS causes on genital nerves are called the primary MS. The ones that develop due to the physical changes MS causes and due to the side effects of drugs are called the secondary MS. And, the sexual dysfunctions that develop based on psychosocial and cultural effects are called the tertiary MS. In MS, decreased libido may be observed in both sexes. Primary sexual dysfunctions in women are decreased vaginal sensation, vaginal dryness, decreased orgasmic capacity, and decreased libido. Secondary sexual dysfunctions are fatigue, urinary and intestinal problems, spasticity, weakness and inactivity. Tertiary sexual dysfunctions can be considered to be the body image, role reversals, diminished feminine feelings, emotional changes, as well as the shortcomings healthcare professionals experience when having conversations with the patient and receiving information from the patient. Sexual dysfunction in the form of spasticity and

decreased vaginal sensation in the lower extremity are common in women. [11-14]

In MS patients, sexual dysfunctions mostly occur in the chronic stage of the disease. Various studies have reported the rate of sexual dysfunction in women with MS to be 52–77%. [12,13,15] In a study, sexual disorders found in female and male patients with MS were at the rates of 91.2% and 86.4%, respectively. [16] The rate of experiencing dysfunctions in women was found to be 83.1% in another study. [17] Lundberg et al. have reported that 6-40% of women experience dyspareunia; 29-86%, decreased sexual desire; 43-62%, decreased genital sensation; 24-58%, decreased orgasmic capacity; and 12-40% experience vaginal dryness. [18]

Healthcare professionals should have sufficient training to talk sexual life with the patient directly, understand the difficulties experienced by the person who cannot explain his/her sexual problems, and give an effective training and counseling service. It is necessary to encourage patients and allow them to ask questions about their sexual concerns. When nurses collect the sexual anamnesis of patients, they should create an appropriate environment. A nurse should be able to analyze value judgments of the society and the individual well. Reassuring and non-judgmental behaviors should be exhibited, and an eye-contact should be made with the patient. The tone of the voice should be soft and the words should be the same as the ones used by the patient. [16,19,20] Proper treatment of sexual dysfunctions depends on a proper assessment of the symptoms in the clinic and guiding the patient correctly. This is very important for improving the quality of life of MS patients.

MS and CONTRACEPTION

- In studies on methods of contraception in multiple sclerosis, the use of oral contraception (OC) was found not to adversely affect the course of MS. OC can be used if there is no risk of thrombosis, smoking, migraine with

aura, advanced age, or similar personal factors.

- In MS, intra uterine devices can be used unless there are distinct sensory symptoms towards the pelvic region.
- The barrier methods are not sufficiently effective. So, as for healthy people, they are not recommended for women with MS, either. ^[21]

MS and PREGNANCY

The Effect of MS on Pregnancy

- Women with MS are as likely to get pregnant and have healthy children as healthy women.
- MS does not have any effect on miscarriage, birth frequency, congenital malformation and infant mortality.
- The risk of a child's having MS is 3–5% if one of the parents has MS. If both parents have MS, the risk is 30%.
- Prospective studies and other research studies have shown that relapse rates decline especially in the third trimester and increase in the first three months of the postpartum period. The frequency of attacks in the postpartum period is related to the disability level and frequency of attacks in the year prior to pregnancy. No correlation has been found between the relapse rate and birth trauma, the type and dose of the anesthesia administered during delivery, breastfeeding, being unable to sleep, or socio-economic factors.
- Magnetic resonance imaging can be used in MS patients after the third month of pregnancy. Contrast agent should not be administered unless necessary. ^[21]
- It has been deemed appropriate to discontinue drugs that are used before (at least one month in advance) the pregnancy planning period. Since there is no information regarding the safety of using the medicine called Natalizumab, patients receiving this treatment should use contraceptive methods and stop using the medicine three months before the period planned for pregnancy. ^[21,22]
- According to data from studies, immunomodulator (IMT) should be ceased before a woman with MS gets pregnant. If a patient gets pregnant while using medication and wants to continue the pregnancy, abortus is not necessary, provided that the medication is ceased. Fingolimod, the very first medicine used orally in the treatment of multiple sclerosis, is recommended to be ceased at least two months before getting pregnant. Azathioprine is among medicines that are relatively safe to use during pregnancy. Methotrexate, however, is associated with miscarriage and the risk of disability in infants and should not be used during pregnancy. ^[21]
- If a severe relapse occurs during pregnancy, a short-term (3-5 day) methylprednisolone (in the FDA-approved C category) treatment is recommended 1 g/day/IV. The use of steroids is not recommended unless there are severe attacks in the first three months. Its use is safer in the second and the third trimesters. ^[21]
- It has been reported that use of interferons (IFN) in pregnancy will not cause major affects because their large molecular dimensions cannot pass through the placental barrier. If immunosuppressants are being used, the medicine should be ceased at least 6 months before pregnancy. ^[21]
- In the presence of serious sensory disorders and paralysis, the pregnant woman with MS may not be able to feel the initiation of contractions, or the induction of delivery may be necessary. Therefore, the patient must be closely monitored throughout the last month, and the birth should be performed in the hospital. Interventions with vacuum, forceps or similar tools and obstetric complications (postpartum hemorrhage) during delivery are more common in MS patients than in normal population. Low birth weight, short stature, or similar conditions are slightly higher than the normal. ^[22]

The Effect of Pregnancy on MS

Two-thirds of patients with multiple sclerosis are women at childbearing ages and approximately 10% of the disease cases start during the pregnancy period; these have led to the discussion of the effect of pregnancy on MS. In 1950s, patients were recommended not to get pregnant because it was believed based on case reports and limited retrospective studies that pregnancy worsens the prognosis of the disease. It was first shown by Douglas and Jorgensen in 1948 that MS does not have any harmful effects on pregnancy and fetus and, unlike what is known, it is not necessary to terminate pregnancy in MS patients. [22,23]

The first study to investigate the course of MS in pregnant women was The Pregnancy in Multiple Sclerosis Study (PRIMS). Confavreux et al. followed 254 patients with relapsing MS in 269 pregnancy periods. They recorded a 70% of decline in attacks in the 3rd trimester compared to the year prior to pregnancy. They observed a 70% of increase in the first 3 months of the postpartum period, compared to pre-pregnancy. This result was associated with immunosuppression in the 3rd trimester and with immune reactivation in the postpartum period. Another result of the same study was that pregnancy did not affect the progress of the disease when the pre-pregnancy year, pregnancy, and the post-pregnancy year were considered altogether. [22,24] Vukusic et al. [25] followed up the patients of the PRIMS study for 2 years. They found that the patients who had high pre-pregnancy disease activity and had attacks during pregnancy had a higher frequency of attacks during the postpartum period. Breastfeeding and epidural anesthesia did not have any significant effect on the prognosis of disease in this group, which was followed up for two years. [22,25]

T helper (Th) cell subgroups are in balance in the organism. Th1 response is the cellular immune component and is responsible for tissue rejection, whereas Th2 response ensures humoral immunity and the release of anti-inflammatory cytokines. In

pregnancy, cytokines secreted by the fetal-placental structure causes the down-regulation of the release of cytokines mediating the cellular immune system by the mother. Consequently, pregnancy is characterized by reduced cellular immunity, increased humoral immunity and the transformation of the balance from Th1 to Th2. Birth is associated with the reversing of this balance at a pronounced level, that is, with the transformation of the Th1 response into a dominant form. This may explain the reduction of attacks in MS patients during pregnancy periods, and increase of attacks after delivery. [25] The reduction in risk of relapses during pregnancy has been linked to rises and falls of estrogen and progesterone levels. A fast Th1 activity occurs in the early period after delivery. For this reason, the frequency of attacks increases by three-fold in this period. Light and traceless attacks occur during pregnancy. However, the attacks after delivery are severe. [26]

Women with MS experience less fatigue and sensory symptoms during pregnancy, whereas some of them express that depressive symptoms increase. Intestinal and bladder problems are common, which may be explained by the constipation and urinary retention due to the pressure on the womb during pregnancy. [22]

Attacks in Pregnancy

The course of MS during pregnancy is better. When considered altogether, MS does not have any adverse effects on pregnancy, delivery and the postpartum period. [22, 27]

According to the results of studies on pregnancy, no adverse effects of MS have been observed on infants. The commonly held view is that attacks diminish during pregnancy but are frequent after delivery, especially between the 3rd and 6th months. High-dose corticosteroids are the drugs to prefer first to treat attacks in pregnancies in MS. Although it is known that corticosteroids pass through the placenta, most of the prednisolone and hydrocortisone is converted by the placenta

into more active metabolites, which reduces fetal steroid concentration to approximately 10% of that of mother. [22,27] No cases of prematurity or low birth weights have been reported to develop due to use of steroids. However, it should be known that steroids may cause neonatal orofacial malformations, and, although rarely, fetal adrenal suppression in the hours following the birth. [22,27,28]

MS and Birth

The National Multiple Sclerosis Society has compared the frequency of attacks experienced by women who gave birth through epidural or general anesthesia and found no significant difference. The frequency of attacks was observed to increase after procedures performed through spinal anesthesia. Therefore, spinal anesthesia should not be preferred in patients with MS. [22, 29]

The forms of birth (cesarean or vaginal deliver) have no effect on attacks or disabilities. Usually, MS does not affect birth, and regular birth can be performed. No correlation has been found between the relapse rate and birth trauma, the type and dose of the anesthesia administered during birth. The MS study group recommends that general anesthesia should be preferred to epidural anesthesia. [21] Perioperative stress and anesthesia also increase the frequency of attacks. This is thought to be linked to developing infections, emotional imbalances and fever, rather than the anesthesia itself. [22, 30]

Initial phases of delivery progress normally in MS patients whose legs and abdominal muscles are weak. Help may be necessary for mothers to be able to push the baby in subsequent phases of delivery. Studies have shown an increase in the rates of interventions with vacuum and forceps and cesarean sections in MS patients due to fatigue, weakness in the legs and contractions. [30]

MS, POSTPARTUM PERIOD and BREASTFEEDING

It is still not clear how breastfeeding affects postpartum attacks. In the postpartum period, the risk of experiencing attacks is around 30%. Breastfeeding alleviates MS inflammations. For this reason, MS patients are recommended to breastfeed their babies during the breastfeeding periods. In two studies conducted in 2009, it was shown that the frequency of postpartum attacks was reduced in women with MS who breastfed for at least 2 months. [22,31,32] In a comprehensive prospective study, it was shown that the frequency of attacks increased in women who did not breastfeed or who breastfed for less than 2 months, but this was not statistically significant. A recent meta-analysis study [34] has shown that breastfeeding mothers are likely to experience half the number of attacks experienced by mothers who do not breastfeed. Today, mothers are usually recommended to breastfeed. However, mothers with high pre-pregnancy disease activity are not able to breastfeed since they are subject to disease modifying therapies (DMTs) immediately after delivery. [22,33]

None of the treatments of Avonex, Betaferon, Copaxone, Rebif, Tysabri and Mitoxantrone has been granted safety approval for use in the breastfeeding period. Steroid treatments can be given by taking certain precautions in the treatment of attacks. If the mother is breastfeeding her baby, she can pump her milk and give it to the baby using a bottle before the administration of corticosteroids, or 4 hours after the administration of steroids. It is not recommended to start administering IMT to patients in the lactation period since the available data are not sufficient. However, in patients with high pre-pregnancy disease activity and attack frequency, early onset of treatment is recommended in the postpartum period. [21,22] If the mother is not going to breastfeed her baby for any reason, the long-term MS treatment can be resumed. [30]

MS and TEST TUBE BABY TREATMENT

Infertility in multiple sclerosis patients is in the same proportion as in normal population. Pregnancies should be planned after appropriate precautions are taken for women with MS. However, patients are known to be interested in using assisted reproductive techniques (ART) because of the difficulty of conception that is reported in MS. [35] In vitro fertilization (IVF) is the fertilization by the combination of sperm and oocyte cells in a culture medium to form embryos to be transferred into the mother's uterus. This technique is administered as a solution to infertility if there are severe sperm disorders and if the tubes are clogged and the number of eggs is low. Michel et al. conducted the largest cohort analysis on the "risk of development of relapses based on IVF" in 32 MS patients. It was reported in that study that relapse rates statistically increased in MS patients after IVF, and this might partially be due to the failure of IVF as well as the use of GnRH agonists. [22,35] In vitro fertilization treatment increases the activity of the disease and the frequency of attacks. [21]

The reasons why the frequency of attacks increase during IVF include the reduction of estrogen during hormonal stimulation, the temporary cessation of immunomodulator treatments, and the stress caused by assisted reproductive techniques. [22,36] MS patients whose fertility has declined and who are considered to be directed to ARTs should definitely be informed about the likelihood that ARTs may increase the risk of attacks. [22,37] MS patients should be aware of the likely increase in the risk of MS attacks, if the procedure does not result in pregnancy after IVF. [22]

MS and MENOPAUSE

There are limited number of studies in the literature drawing attention to the relationship between MS and the menopause period. It has been reported that

in MS, estrogen might affect Th1 and Th2 lymphocyte levels and, therefore, the ratio of Th1 to Th2. It has also been reported that hormonal changes during the transitional periods such as pregnancy and menopause at different phases of menstrual cycle might affect the activity of the disease. [38] It has been well-known for long that MS attacks decline during pregnancy in the 3rd trimester, which is characterized by high estrogen levels and that attacks increase by 2–3-fold in the postpartum period, which is characterized by a sudden withdrawal of estrogen levels. [38,39]

In a study on 90 women with MS who were in the postmenopausal period, 54% of women were found to have symptoms that worsened with menopause, and 75% of those who tried the hormone replacement therapy (HRT) were found to experience an improvement. [40] In another study, 72 postmenopausal women were examined and it was found that with menopause, MS symptoms did not change in 55% of the cases, increased in 40% of the cases, and decreased in 5% of the cases. [39] Differently from the above study, it was also found that 55% of 30 women receiving HRT did not experience any change in the symptoms, 41% had worse symptoms, and 4% had better symptoms. [39] In this study, patients were assessed retrospectively, and information such as the stage of menopause when the change in MS symptoms took place and the type of HRT was not specified. [38,39] In a case study carried out by Kurt et al., [41] the clinic of the patient progressed rapidly after menopause, and the patient became wheelchair dependent. This patient was planned to continue treatment with azathioprine, which is a wide-spectrum immunosuppressant and whose clinical efficacy has been shown in many studies in patients with remitting MS and progressive MS. [41]

In their study, Bove et al. [42] found that the physical qualities of life increased in MS patients who used regular hormone therapy during their postmenopausal period.

They suggested that different studies should be carried out on the subject.

CONCLUSION

In conclusion, MS treatment and care plans should be created by taking into account the different stages of woman's health. In this disease, which still has mysterious aspects, the treatment and training programs to be given by healthcare professionals and nurses to patients, their husbands and families should be applicable and have traceable outcomes. A proper counseling given to women with MS should not just include the organization of treatment, it should also include on time interventions in unfavorable situations and patients' development of their own awareness. It is thought that for the benefit of MS patients, is also important to decide - together with the patient - rehabilitation treatments such as exercise and relaxation programs that are medically and clinically appropriate and are supported in the literature. These should all be done by taking into account the natural processes of pregnancy, breastfeeding and woman's life. It is also very important for MS to ensure continuity of treatment and clear communication. Treatment programs planned according to personal differences of being a woman will build families with better quality of life.

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How to cite this article: Doğan HD. Multiple sclerosis and to be woman. Int J Health Sci Res. 2018; 8(7):352-359.
