Multiple sclerosis in pregnancy

Essay

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By

Ahmed Lotfy Abdelaziz Moustafa
M.B., B.Ch.

Under Supervision of

Prof. Mahmoud Hemida El-Rakawy
Professor of Neuropsychiatry
Faculty of Medicine
Ain Shams University

Dr.Hala Mahmoud El-khawas
Assistant professor of Neuropsychiatry
Faculty of Medicine
Ain Shams University

Dr.Yousry Abo-El Naga Abd El Hamid
Assistant professor of Neuropsychiatry
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
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مرض التصلب المتعدد و الحمل

توطئة

للحصول على درجة الماجستير في طب المخ و الأعصاب و الطب النفسى

مقدمة من الطبيب

أحمد لطفي عبد العزيز مصطفى

تحت إشراف

الأستاذ الدكتور محمود حميدة الرقاوى

استاذ طب المخ و الأعصاب و الطب النفسى

كلية الطب

جامعة عين شمس

الدكتورة هالة محمود الخواص

استاذ مساعد طب المخ و الأعصاب و الطب النفسى

كلية الطب

جامعة عين شمس

الدكتور يسري أبو النجا عبد الحميد

استاذ مساعد طب المخ و الأعصاب و الطب النفسى

كلية الطب

جامعة عين شمس

كلية الطب

جامعة عين شمس

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Summary

Multiple sclerosis most often occurs in women of child-bearing age. Therefore, patients are often faced with dilemmas surrounding pregnancy **(D'hooghe *et al.*, 2010).** Although Women can be reassured that multiple sclerosis usually has no negative impact on fertility or the rate of fetal abnormality **(Stuart and Bergstrom, 2011)**, research has found that childlessness and termination of pregnancy remain higher in the multiple sclerosis population **(Prunty *et al.*, 2008)**. Lack of knowledge in female multiple sclerosis patients concerning the interactions of multiple sclerosis and pregnancy is evident **(Albrecht *et al.*, 2010)**.

Main themes proposed to capture the key aspects of how women managed motherhood in relation to their experience of multiple sclerosis include firstly infertility**.** Women with multiple sclerosis can have infertility issues at a rate consistent with the normal age-matched population. To date, there are too few cases of in vitro fertilization in multiple sclerosis to warrant firm conclusions. Anecdotal reports suggest that in vitro fertilization may be associated with an exacerbation of relapse in multiple sclerosis **(Laplaud *et al.*, 2007)**. Larger studies are needed to determine whether certain forms of in vitro fertilization indeed exacerbate multiple sclerosis **(Voskuhl, 2010)**.

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Ahmed Lotfy

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Introduction

Multiple sclerosis is an autoimmune disease of the central nervous system (CNS), which results in a chronic focal inflammatory response with subsequent demyelination and axonal loss. It usually begins with acute episodes of neurological dysfunction, the relapses, followed by periods of partial or complete remission. This relapsing-remitting phase is usually followed by a steady, continuous and irreversible worsening of the neurological dysfunction, which characterizes the progressive phase of the disease **(Vukusic *et al.*, 2009).**

Multiple sclerosis is the most common disabling central nervous system disease of young adults, and its prevalence in the western world is ~1 in 1000. Among adults with multiple sclerosis, the female-to-male ratio is ~2 to 1, and the majority (~80%) received their diagnosis between the ages of 20 and 45 years) **(Keegan and Noseworthy, 2002)**. Therefore, women of reproductive age are commonly affected. Pregnancy modulates the disease activity of multiple sclerosis and also alters the course of several other autoimmune diseases, including uveitis, thyroiditis, and rheumatoid arthritis **(Saraste *et al.*, 2007)**.

Like these various other autoimmune disorders, multiple sclerosis normally improves during pregnancy. Pregnant multiple sclerosis patients experience a significant reduction in relapse rates and magnetic resonance disease activity **(Ehrlich *et al.*, 2007).**

It is yet unclear, which immuno-endocrinological processes mediate these disease fluctuations. Leptin, for example, has been identified as a hormone that can influence inflammatory activity as it is increased during late pregnancy, and the post-delivery drop was associated with the occurrence of postpartum relapse **(Neuteboom *et al*, 2009)**. The relapse rate after pregnancy does not mean an increased risk for exacerbation, but rather, a return to pre-pregnancy level within 3 months postpartum **(Haas and Hommes, 2007).**

These clinical observations also illustrate an effect of sex hormones on disease suggesting potential use of hormones for treatment of multiple sclerosis. A growing number of studies support a therapeutic effect of these hormones **(Gold and Voskuhl, 2009)**. On the whole, the existing epidemiologic evidence does not support an important effect of oral contraceptive use on the risk of multiple sclerosis, though it does suggest that oral contraceptives might delay the onset of the disease **(Alonso and Clark, 2009).**

The currently approved treatments for relapsing–remitting multiple sclerosis (Interferon-β; Glatiramer Acetate and Mitoxantrone) as well as emerging therapies including monoclonal antibodies (such as Natalizumab, Alemtuzumab, and Rituximab) and oral drugs currently in Phase III trials (Cladribine, Fingolimod (FTY 72), Teriflunomide, Oral fumarate, and Laquinimod) all target the inflammatory component

of multiple sclerosis pathogenesis. While these may exert some indirect neuroprotective effects via inhibition of inflammation, there are no directly neuroprotective agents available at this time. Direct neuroprotection would involve a treatment that could cross the blood brain barrier to promote the health of neurons, axons and oligodendrocytes directly, not merely reduce inflammatory cell infiltration into the brain **(Gold and Voskuhl 2009).**

Although the immunomodulatory therapy for treatment of multiple sclerosis in pregnancy does not constitute a major risk for prenatal developmental toxicity **(Weber-Schoendorfer and Schaefer, 2009)**, among infants exposed to immunomodulators in utero, a higher rate of birth defects than those not exposed was found. The reduction in multiple sclerosis relapses during second and third trimester of pregnancy and its increase during postpartum is the rule **(Fernández Liguori *et al*, 2009).** Discontinuation of immunomodulatory therapy before conception, and resumption shortly after delivery was the most frequent clinical practice procedure. Again, Accidental exposure to immunomodulatory therapy did not affect pregnancy outcomes or increased malformation rates. **(De Las Heras *et al*, 2007).**

The motherhood decision for women with chronic illnesses/disabilities is not an easy decision. Such women often view motherhood as 'risky'. Prior to 1950, the general consensus was that pregnancy accelerated the course of multiple sclerosis and women were discouraged from becoming pregnant. When pregnancy

occurred, a termination was often recommended. There is now consensus, based on large prospective studies, that pregnancy in multiple sclerosis neither exacerbates the illness nor is a risk to the child. Despite this changing evidence, higher rates of termination of pregnancy and childlessness continue for women with multiple sclerosis than for the general population and pregnant women with multiple sclerosis continue to view pregnancy as risky **(Prunty *et al.*, 2008)**.

Pregnancy does not seem to pose a woman with multiple sclerosis to a greater risk for pregnancy complications when compared with women in general. The potential need for instrumental delivery should, however, be taken into account when planning the delivery of a mother with multiple sclerosis **(Jalkanen *et al.*, 2010).** This however, highlights a need for more intensive monitoring and obstetric care during pregnancy, so, more information can be provided to affected women concerning pregnancy **(Chen YH *et al.*, 2009).** The complete information must include data regarding the effect of multiple sclerosis on pregnancy and child-rearing and the effect of pregnancy on multiple sclerosis and its progression need to be made more accessible to women **(Prunty *et al.*, 2008)**[2]

Aim of the Work

To review the updates in the clinical and management profile of Multiple Sclerosis in affected women before, during and after pregnancy.

1

Multiple sclerosis: General Considerations

Introduction

Multiple sclerosis is a potentially highly disabling disorder with considerable social impact and economic consequences. It is the major cause of non-traumatic disability in young adults. The social costs associated with multiple sclerosis are high because of its long duration, the early loss of productivity, the need for assistance in activities of daily living and the use of immunomodulatory treatments and multidisciplinary health care **(Leray *et al.*, 2007)**.

Epidemiology

Multiple sclerosis has a prevalence that ranges between 2 and 150/100,000 depending on the country or specific population. Studies on population and geographical patterns of epidemiological measures have been very common in multiple sclerosis, and have led to the proposal of different etiological theories. Multiple sclerosis usually appears in adults in their thirties, but it can also appear in children, and in people over fifty as well **(Koutsouraki *et al.*, 2010)**.

Like other autoimmune disorders, the disease is more common in women, and the trend may be increasing. The overall incidence rate of multiple sclerosis is 3.6