Misconceptions about multiple sclerosis and pregnancy in the Qassim region in 2021-2022: a cross-sectional study

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Abstract. – OBJECTIVE: Multiple sclerosis (MS) is a disease with higher female prevalence, and the majority of patients are of childbearing age. Thus, pregnancy concerns are important for patients with MS and their families. Improving the understanding of the effects of pregnancy on the progress of MS could improve the knowledge about pregnancy-related issues in MS patients. The aim of this study is to evaluate the general knowledge of Saudi adults living in the Qassim region regarding pregnancy-related relapses in relapsing-remitting MS (RRMS) and to identify misconceptions regarding pregnancy, breastfeeding, and the use of oral hormonal contraceptives among female MS patients.

SUBJECTS AND METHODS: A representative random cluster sample of 337 participants was used in this cross-sectional study. All participants were living in one of the following cities in the Qassim region: Buraydah, Unaizah, and Alrrass. Data collection was done between February 2022 and March 2022 using a self-administered questionnaire.

RESULTS: The overall mean knowledge score was 7.42 (SD 4.21), with poor, moderate, and good knowledge representing 77.2%, 187%, and 4.2% of the sample, respectively. Higher knowledge scores were associated with age less than 40 years, being a student, knowing about MS, and knowing someone with MS. Other variables such as gender, educational level, and residence location did not show significant differences regarding the knowledge score.

CONCLUSIONS: Our results demonstrate that knowledge and attitude are suboptimal among the Qassim population regarding the effects of MS on pregnant patients, pregnancy outcomes, breastfeeding, and usage of contraceptive methods, with 77.2% showing poor total knowledge scores.

Key Words:

Pregnancy, Multiple sclerosis, Childbearing.

Introduction

Multiple sclerosis (MS) is an inflammatory disease that disturbs the central nervous system¹. The etiology of the disease is not precisely known yet, but research suggests an association between environmental factors such as infectious agents, sun exposure/vitamin D deficiency, and the risk of developing MS in the presence of genetic susceptibility to the disease². As a major long-lasting chronic neurological disorder, it requires extensive healthcare as well as public awareness programs.

Layers of fat cells called myelin sheaths enclose nerve axons. Throughout the course of MS, myelin sheaths are physically and functionally impaired by the action of the body's immune system, resulting in demyelination and axonal deterioration³. Dysfunction of the nervous system results in symptoms that differ broadly among individuals and often include blurry vision, "pins and needles" sensation (paresthesia), numbness (hypoesthesia), impaired balance (ataxia), declined cognitive function, muscle weakness/spasms, problems with verbal communication (dysarthria), and lethargy^{4,5}.

The clinical course of MS can be used to classify the disease into four clinical patterns: relapsing-remitting MS (RRMS), primary progressive MS (PPMS), secondary progressive MS (SPMS), and progressive relapsing MD (PRMS)^{6,7}. RRMS is the most common form, and nearly 87% of MS patients fall under this classification⁶. It is characterized by acute relapses separated by longer periods of recovery and cessation of disease progression^{6,7}.

The diagnosis of MS relies heavily on medical history, neurological assessment, MRI, lumbar puncture for cerebrospinal fluid (CSF), evoked

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potentials, and blood work8. According to the Atlas of MS, there is a prevalence of 2.8 million diagnosed MS patients worldwide⁹, 80% of MS patients are 20 to 45 years old, and there is a greater impact on women with a female-to-male ratio of 2.59,10. Improved access to healthcare, later childbirth, hormonal replacement therapy, obesity, and smoking are possible underlying causes for the gender disparity in MS. However, vitamin D deficiency is the most plausible theory for this disproportionate rise of MS among females11. Recent epidemiological studies revealed a notable increase in MS prevalence in the Kingdom of Saudi Arabia (KSA)¹². The vast majority of diagnosed MS individuals are women in their fertile years¹⁰, and concerns have been raised about conception, pregnancy, lactation, and motherhood in relation to relapses of MS.

The literature provides adequate data about MS prevalence along with clinical outcomes of the disease in relation to pregnancy, breastfeeding, and oral contraceptives. However, there are insufficient data regarding the knowledge, attitude, and practices of the general public in the Qassim region concerning family-planning matters such as birth control, pregnancy, and lactation among women with MS. As having a family is an essential part of life in our culture, we aim to bring attention to MS and motherhood. Therefore, this community-based study was done to determine the extent of awareness among the Qassim population about pregnancy-related relapses in RRMS in addition to misconceptions regarding MS and childbearing-related issues.

Subjects and Methods

This community-based cross-sectional descriptive study was conducted in the region of Qassim, KSA, between February 2022 and March 2022. Relevant approval for the study was obtained from the Qassim Region Research Ethics Committee. We used a convenience non-probability sample, and out of the 11 cities in the Qassim Region, we selected the main ones: Buraydah, Unaizah, and Alrrass. The inclusion criteria were Saudi adults aged ≥20 years who agreed to participate in the study. The exclusion criteria were people under the age of 20 years.

The study involved 337 participants. Data were collected using a validated questionnaire after obtaining consent from the original authors¹³ (**Appendix 1**). The questionnaire was divided into 3

sections. The first one was about participants' sociodemographic characteristics, including age in years, gender, educational level, employment status, residence, whether they know what MS is, and whether they know someone who has MS. The second one was about participants' sources of information on MS, such as the internet or social media, family, friends, or neighbors, healthcare workers, or other sources (education programs on TV or radio, and MS information leaflets, brochures, or posters). The third section was on participants' knowledge of MS.

The questionnaire was divided into two parts. The first part contained eight close-ended questions in Arabic covering the system affected by MS, the groups mostly affected by MS based on age and gender, the cause of MS, risk factors increasing the risk of MS, symptoms of MS, whether there is a definitive cure for MS, and the availability of medications that can control the symptoms. The second part was about MS during pregnancy and contained seven close-ended questions about the danger of MS for pregnancy and its completion, the effect of MS on pregnancy and fetus health, whether there is a safe medication for MS during pregnancy, pregnancy's impact on the health of mothers who have MS, MS and breastfeeding, and the usage of oral contraceptive pills among MS patients. All participants were volunteers and had the right to refuse to participate in the study. Participant data were kept confidential and only used for the purposes of the research.

Statistical Analysis

The answers were coded as "correct" (1 point) or "false" (0 points). Questions 13 and 14 were multiple-response questions with 5 and 4 correct answers, respectively. The total knowledge score was calculated by adding all 22 items' scores. We collected the correct answers to the 15 questions for each participant. A participant was considered to have poor knowledge if their score was <11, whereas a participant with a score ≥17 was considered to have good knowledge. The cut-off points were selected based on the agreement of statisticians to represent the level of knowledge.

The difference in the knowledge scores according to the sociodemographic characteristics of participants was analyzed using a Mann-Whitney Z-test and Kruskal-Wallis H-test. The questionnaire was pretested in a pilot study using a sample of 35 participants, but their results are not included in the current study. A *p*-value of 0.05

was considered statistically significant. A Shapiro-Wilk test was performed to test the normality of data. The knowledge score followed an abnormal distribution, so non-parametric tests were applied. All data analyses were performed using the Statistical Packages for Software Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA).

Results

There were 337 respondents who replied to our survey, and Table I describes their socio-demographic characteristics. The most common age group was 20-29 years (48.4%), and there were more females than males (75.4% vs. 24.6%). Most participants had bachelor's degrees (74.5%), and 43% were working. Respondents who were living in Alrass constituted 43% of the population. The prevalence of participants who knew about MS was 77.4%, while the prevalence of respondents who knew someone with MS was 35%. The most common sources of MS information were the internet or social media (66.2%), followed by family, friends, neighbors (36.5%), and health workers (11.5%) (Figure 1).

An assessment of the knowledge about MS is shown in Table II. Respondents knew that the most common system affected by MS was the central nervous system (75.4%), 39.8% were

Table I. Participants socio-demographic characteristics (n=337).

Study variables	N (%)
Age group	
• 20-29 years	163 (48.4%)
• 30-39 years	59 (17.5%)
• 40-49 years	64 (19.0%)
• 50-59 years	38 (11.3%)
• ≥60 years	13 (03.9%)
Gender	
• Male	83 (24.6%)
• Female	254 (75.4%)
Educational level	
 Primary school 	13 (03.9%)
 Secondary school 	56 (16.6%)
 Bachelor's degree 	251 (74.5%)
 Postgraduate 	17 (05.0%)
Employment status	
• Student	94 (27.9%)
• Employed	147 (43.6%)
 Unemployed 	96 (28.5%)
Residence location	
 Alrass 	145 (43.0%)
 Onaizah 	35 (10.4%)
 Buraidah 	130 (38.6%)
• Other	27 (08.0%)
Do you know what multiple sclerosis is?	
• Yes	261 (77.4%)
• No	76 (22.6%)
Do you know someone who has MS	
(relatives, friends)	
• Yes	118 (35.0%)
• No	219 (65.0%)

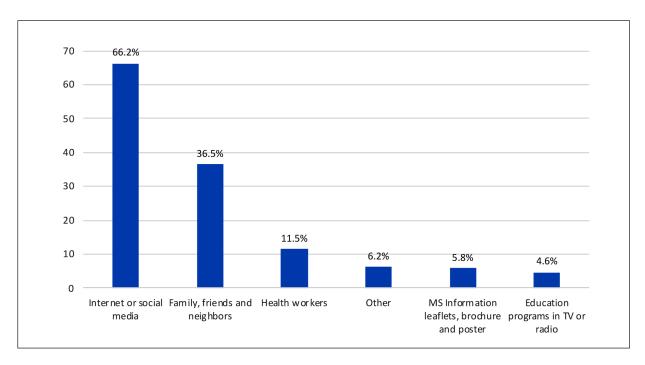


Figure 1. Sources of MS information.

Table II. Assessment of the knowledge about MS (n = 337).

Knowledge statement	N (%)
1. Which system is affected by multiple sclerosis?	
Respiratory system	06 (01.8%)
Central nervous system*	254 (75.4%)
Musculoskeletal system	26 (07.7%)
Circulatory system	01 (0.30%)
• I don't know	50 (14.8%)
2. Which age group is affected by Multiple sclerosis?	
• 0-19 years	20 (05.9%)
• 20-39 years*	134 (39.8%)
• 40-59 years	37 (11.0%)
• \geq 60 years	09 (02.7%)
• I don't know	137 (40.7%)
3. Who is affected more by multiple sclerosis?	,
Females*	147 (43.6%)
• Males	20 (05.9%)
• Equal	44 (13.1%)
• I don't know	126 (37.4%)
	120 (37.470)
4. What is the cause of multiple sclerosis?	
Meningoencephalitis	98 (29.1%)
Atherosclerosis	15 (04.5%)
Immunodeficiency	38 (11.3%)
• Evil eye	05 (01.5%)
• Unknown*	82 (24.3%)
• I don't know	99 (29.4%)
5. What are the risk factors that increase the development of multiple sclerosis? [†]	
Vitamin D deficiency*	125 (37.1%)
Personal history of autoimmune diseases*	119 (35.3%)
Family history of multiple sclerosis*	72 (21.4%)
Sedentary lifestyle	26 (07.7%)
• Viruses*	21 (06.2%)
• Obesity*	14 (04.2%)
High levels of Growth hormone	13 (03.9%)
Hypertension	10 (03.0%)
• I don't know	114 (33.8%)
6. What are the symptoms of multiple sclerosis? [†]	` '
Paralysis or weakness*	235 (69.7%)
Numbness*	150 (44.5%)
Blurred and double vision*	` ′
	102 (30.3%) 70 (20.8%)
 Difficulty concentration and memorizing* Breathing difficulties 	24 (07.1%)
Fever	20 (05.9%)
• Palpitations	12 (03.6%)
Common cold symptoms	02 (0.60%)
I don't know	59 (17.5%)
	39 (17.370)
7. Is there a cure for multiple sclerosis?	,
• Yes	71 (21.1%)
• No	124 (36.8%)
• I don't know	142 (42.1%)
8. Are there medications that can control multiple sclerosis symptoms?	
• Yes	206 (61.1%)
• No	11 (03.3%)
• I don't know	120 (35.6%)
9. Does multiple sclerosis pose any risk to the health and completion of pregnancy?	
Yes Yes	92 (27.3%)
• Yes • No	70 (20.8%)
• I don't know	` /
1 WOLL & KHOW	175 (51.9%)

Table II *(Continued)*. Assessment of the knowledge about MS (n = 337).

Knowledge statement	N (%)
10. In your opinion, what is the impact of MS on pregnancy?	
Positive impact	29 (08.6%)
Negative impact	187 (55.5%)
MS does not have any effect on pregnancy at all*	121 (35.9%)
11. How does MS affect pregnancy in your opinion?	
Delay conception	20 (05.9%)
Repeated abortions	71 (21.1%)
Fetal malformations	24 (07.1%)
MS does not have an impact on the health of the mother or the fetus, however,	201 (59.6%)
the mother will have a relapse after delivery if she did not get the proper medical plan*	
• Others	21 (06.2%)
12. Among MS medications, is there some that are proven to be safe during pregnancy?	
• Yes	78 (23.1%)
• No	31 (09.2%)
• I don't know	228 (67.7%)
13. What is the effect of pregnancy on the health of a female MS patient?	
Leads to repeated relapses during the pregnancy period	160 (47.5%)
Pregnancy has a protective effect against MS attack (honeymoon period) *	67 (19.9%)
• No effect	110 (32.6%)
14. Is being an MS patient causing any problems with breastfeeding?	, ,
Yes	46 (13.6%)
• No	68 (20.2%)
• I don't know	223 (66.2%)
	(***_/*)
15. Can an MS patient use hormonal contraceptive methods? • Yes	39 (11.6%)
• No	44 (13.1%)
• I don't know	254 (75.4%)
- 1 doil t know	234 (73.470)
Total knowledge score (mean ± SD)	7.42 ± 4.21
Level of knowledge	
Poor	260 (77.2%)
Moderate	63 (18.7%)
• Good	14 (04.2%)
	= : (3 ::270)

[†]Variable with multiple response answers. *Indicates correct answer.

aware that the most common age group affected was 20-39 years, and females were perceived as being more affected than males (43.6%). Furthermore, 24.3% were aware that the cause of MS is unknown. Respondents rated vitamin D deficiency (37.1%), personal history of autoimmune diseases (35.3%), and family history of MS as the most common risk factors for the development of MS, while paralysis or weakness (69.7%), numbness (44.5%), and blurred vision were considered as the most common symptoms of MS.

Only 36.8% believed that there is no cure for MS, although 61.1% believed that there were medications to control the symptoms. When asked whether MS poses any risk to the health and completion of pregnancy, 27.3% agreed that

it does, while 20.8% did not agree. Furthermore, 35.9% of the respondents believed that MS does not have any effect on pregnancy. When asked how MS affects pregnancy, 59.6% indicated that MS does not have an impact on the health of the mother or the fetus, but the mother will have a relapse after delivery if she does not receive proper medical treatment.

Only 23.1% believed that MS medications are proven to be safe for pregnant women, and only 19.9% believed that pregnancy has a protective effect against MS attacks. Approximately 13.6% believed that MS could potentially cause problems with breastfeeding, while 20.2% did not believe it. In addition, only 11.6% believed that MS patients can use hormonal contraceptive methods.

Based on the given criteria, the overall mean knowledge score was 7.42 (SD 4.21), with poor, moderate, and good knowledge representing 77.2%, 187%, and 4.2% of the population, respectively. As shown in Table III, a higher knowledge score was more associated with being younger than 40 years of age (Z=4.314; p<0.001), being a student (H=16.270; p<0.001), knowing about MS (Z=8.356; p<0.001), and knowing someone with MS (Z=3.711; p<0.001). Other variables such as gender, educational level, and residence location did not show significant differences in terms of knowledge scores.

Discussion

MS is an autoimmune demyelinating disease of the central nervous system. This study examines the awareness of the impact of pregnancy on the disease in the Qassim region. The average MSQ score among all the participants was 7.42±4.21, which indicates a very poor level of knowledge. The low level of education about the disease can

be clarified by the characteristics of MS, which are unpredictable and may manifest with various symptoms, meaning many people may not understand the disease.

The study results are comparable to those of other local studies¹⁴⁻¹⁶ with different study designs done in Jeddah, Taif, and Riyadh, which also had poor results. In the present study, almost three-fourths of the participants were females, and only 43.6% of the subjects knew what gender is affected more by MS. However, this result was lower than results from a study¹⁶ in Taif, in which 70% of the subjects knew about this fact.

We found that there was a significant relation of knowledge with being less than 40 years of age and knowing someone with MS. Unfortunately, there was no significant relationship between educational level and knowledge score. This shows that there was no specific distribution of the awareness level in terms of residence or gender. This was unlike the study¹⁵ done in Jeddah, which showed a significant relationship between educational level and knowledge score, as expected.

Table III. Differences in the score of knowledge according to the socio-demographic characteristics of participants (n=337).

Factor	Knowledge Score (20) mean ± SD	Z/H-test	<i>p</i> -value
Age group ^a			
• < 40 years	8.13 ± 4.29	Z = 4.314	< 0.001**
• \geq 40 years	6.03 ± 3.71		
Gender ^a			
• Male	7.37 ± 3.69	Z = 0.029	0.977
• Female	7.43 ± 4.37		
Educational level ^a			
 Secondary or below 	6.81 ± 4.48	Z = 1.509	0.131
Bachelor or higher	7.57 ± 4.14		
Employment status ^b			
• Student	8.99 ± 4.44	H = 16.270	< 0.001**
• Employed	7.09 ± 3.98		
Unemployed	6.37 ± 3.92		
Residence location ^b			
• Alrass	7.30 ± 4.09	H = 6.552	0.088
• Unaizah	8.14 ± 3.66		
Buraidah	7.70 ± 4.47		
• Other	5.70 ± 3.95		
Do you know what multiple sclerosis is? ^a			
• Yes	8.44 ± 3.94	Z = 8.356	< 0.001**
• No	3.89 ± 3.07		,,,,,
Do you know someone who has MSa			
• Yes	8.49 ± 3.68	Z = 3.711	< 0.001**
• No	6.84 ± 4.37		****
• Yes	118 (35.0%)		

 ^{a}p -value has been calculated using Mann-Whitney Z-test. ^{b}p -value has been calculated using Kruskal-Wallis H-test. **Significant at p < 0.05 level.

Most contributors knew about the most common system affected by MS and the affected age group. However, most of the participants showed poor knowledge regarding the treatment and etiology, and 29.4% of the subjects' choices for this question were "I don't know." The results are similar to those of the Saudi study¹⁶ performed in Taif. This shows that the cause and treatment of the disease are usually ignored topics and require more education in the community.

55.5% of the subjects believed that MS has a negative impact on pregnancy, which must be taken into account in order to find an appropriate method to raise the awareness. 67.7% of the responders answered "I don't know" in regard to whether there are any medications that are proven to be safe during pregnancy and that should be taken under consideration. 61.1% of responders showed that they have an idea of whether there is a medication that can control MS symptoms, which is a promising result.

Regarding the risk factors, 37.1% of responders chose vitamin D deficiency, and 35.3% chose personal history of autoimmune diseases. The results of the present study are better than the results of the Taif study¹⁶, in which 84% of the responses were "no" for the statement, "There is a role for vitamin D and ultraviolet rays from the sun in protection against MS".

The onset of MS occurs at the age of 20-30 years, when people consider planning a family. Pregnancy may concern the patient and the patient's family about the effects of MS on pregnancy. Raising awareness about the disease and how it affects pregnancy should be considered to reduce the burden of the disease among patients. When the general public is adequately informed about the nature of the disease, it could relieve the pressure on patients who wish to become parents and have their own families.

The association between *in vitro* fertilization (IVF) and the probability of a subsequent MS relapse was examined in a published study¹⁷. 32 MS patients underwent 70 IVF procedures during the course of the 11-year trial, 48 of which used GnRH agonists and 19 of which used GnRH antagonists. The annualized recurrence rate (ARR) significantly increased in the three months post IVF compared to a control period one year prior to IVF. The usage of GnRH agonists and unsuccessful IVF were linked to the considerable rise in relapses. Small cohort was one of the study's limitations, and it is challenging to make firm judgments based on just 32

cases¹⁷. In a more recent study¹⁸, which included 225 women with 338 IVF procedures, it was discovered that there is no increased incidence of relapse following IVF. Women who received treatment up until IVF had a reduced ARR both before and after the procedure.

Vitamin D deficiency is a well-known risk factor for acquiring MS and increases disease activity in people who already have the condition¹⁹. When given the same dose of oral cholecalciferol supplementation, MS patients had a lesser increase in serum 25-hydroxyvitamin D levels than healthy controls19. A published article¹⁹ identified that vitamin D supplementation lowers oxidative stress markers in healthy controls but not in MS patients. There is growing evidence in the literature that vitamin D deficiency contributes to metabolic abnormalities and infertility in polycystic ovarian syndrome patients (PCOS)20. Hence, some studies20 encourage prescribing low doses of vitamin D (400-800 IU/day) especially in PCOS patients who have vitamin D deficiency. On the other hand, a recent meta-analysis²¹ of a randomized, double-blind, placebo-controlled clinical trial concluded that vitamin D did not have any therapeutic effects on disability or relapse rate in MS patients. One study concluded that while myo-inositol alone only seems to boost thyroid function, taking them together with melatonin seemed to have a positive effect on glucose metabolism²². Another study showed that myo-inositol and α-lactalbumin together may decrease insulin resistance and abnormal fetal development in GDM-affected women²³. The treated group showed a decreased incidence of insulin treatment and preterm delivery²³. Animals and plants both generate alpha lipoic acid (ALA), however humans only make very little amounts of the substance²⁴. Red meat is the most important source of ALA for human nutrition (especially liver, kidney, and heart)²⁴. ALA has been shown to have positive effects in a variety of gynecological contexts, particularly in pregnancy-related serious conditions²⁴. Some studies²⁴ hypothesized that ALA, when administered along with myo-Ins, might be helpful in alleviating the symptoms and biochemical characteristics of PCOS²⁴. This hypothesis was supported by the observed impact of ALA on glucose metabolism. However, there is little data to support this claim, and ALA does not appear to have a substantial impact on reproductive hormones²⁴. Its favorable benefits are likely limited to the metabolic characteristics of women with PCOS who are insulin resistant. Even if combined with myo-Ins, ALA should not be advised for routine clinical care of PCOS at this time²⁴.

The sample involved more female participants than males, as expected. The study was conducted in one region of Saudi Arabia, so it cannot represent the whole population of Saudi Arabia.

Conclusions

The findings demonstrate insufficient understanding of the basics of MS, despite the fact that most respondents recognized the common system affected by MS, gender, age group, and common symptoms. Yet our sample showed a lack of general background information about MS and health education. There was suboptimal knowledge and attitude among the Qassim population regarding MS's effects on pregnant patients, pregnancy outcomes, breastfeeding, and usage of contraceptive methods, with 77.2% showing a poor total knowledge score.

The internet and social media were the most common sources of information to seek knowledge about MS in our sample. Therefore, we recommend the utilization of media through campaigns and educational programs to assure that reliable information reaches the public. In addition, more research is required to identify the cause of insufficient knowledge and attitude toward MS and related pregnancy concerns among the population.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethics Approval

Ethics approval for the study was obtained by the Qassim Region Research Ethics Committee (Approval No. 21-07-11)

Informed Consent

All participants were volunteers and had the right to refuse to participate in the study. A written informed consent was taken from each participant.

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Authors' Contribution

Dr Mariam Alharbi supervised this study, all authors participated in manuscript writing, data collection and revision of the final draft.

Data Availability

All data are available upon reasonable request from the corresponding author.

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References

- Noyes K, Weinstock-Guttman B. Impact of diagnosis and early treatment on the course of multiple sclerosis. Am J Manag Care 2013; 19: s321-s331.
- Milo R, Kahana E. Multiple sclerosis: geoepidemiology, genetics and the environment. Autoimmun Rev 2010; 9: 387-394.
- 3) Dobson R, Giovannoni G. Multiple sclerosis a review. Eur J Neurol 2019; 26: 27-40.
- Ben-Zacharia A. Therapeutics for multiple sclerosis symptoms. Mt Sinai J Med 2011; 78: 176-191.
- Beiske A, Pedersen E, Czujko B, Myhr K. Pain and sensory complaints in multiple sclerosis. Eur J Neurol 2004; 11: 479-482.
- Loma I, Heyman R. Multiple sclerosis: pathogenesis and treatment. Curr Neuropharmacol 2011;
 409-416.
- Tullman M. Overview of the epidemiology, diagnosis, and disease progression associated with multiple sclerosis. Am J Manag Care 2013; 19: S15-20.
- Ömerhoca S, Akkaş S, İçen N. Multiple sclerosis: diagnosis and differential diagnosis. Noro Psikiyatr Ars 2018; 55: S1-9.
- Walton C, King R, Rechtman L, Kaye W, Leray E, Marrie R, Robertson N, Rocca N, Uitdehaag B, I, Wallin M, Helme A, Napier C, Rijke N, Baneke P. Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. Mult Scler 2020; 26: 1816-1821.
- Orton S, Herrera B, Yee I, Valdar W, Ramagopalan S, Sadovnick A, Ebers G. Sex ratio of multiple sclerosis in Canada: a longitudinal study. Lancet Neurol 2006; 5: 932-936.
- Sellner J, Kraus J, Awad A, Milo R, Hemmer B, Stüve O. The increasing incidence and prevalence of female multiple sclerosis—a critical analysis of potential environmental factors. Autoimmun Rev 2011; 10: 495-502.
- 12) AlJumah M, Bunyan R, Al Otaibi H, Al Towaijri G, Karim A, Al Malik Y, Kalakatawi M, Alrajeh S, Al Mejally M, Algahtani H, Almubarak A, Cupler E,

- Alawi S, Qureshi S, Nahrir S, Almalki A, Alhazzani A, Althubaiti I, Alzahrani N, Mohamednour E, Saeedi J, Ishak S, Almudaiheem H, El-Metwally A, Al-Jedai A. Rising prevalence of multiple sclerosis in Saudi Arabia, a descriptive study. BMC Neurol 2020; 20: 49.
- 13) Al-Hamdan N, Al-Otaibi E, Al-Mutairi M, Al-Mutairi M, Al-Otaibi O, Al-Mozeri M, Al-Masaud W, Al-Batanony M. Awareness of Saudi community toward multiple sclerosis in Qassim Region, Saudi Arabia. Neurosciences (Riyadh) 2021; 26: 77-84.
- 14) Hudaif H, Bwardi N, Kojan S. Assessment of multiple sclerosis awareness and knowledge among the Saudi population in Riyadh City. Mult Scler Relat Disord 2014; 3: 758.
- 15) Farran E, Waggas D, Alkhunani T, Almuwallad S, Aljohani R. Assessment of Multiple Sclerosis Awareness and Knowledge among the Community of Jeddah, Saudi Arabia. J Neurosci Rural Pract 2021; 12: 733-738.
- 16) Amer M, AlZahrani W, AlZahrani A, Altalhi F, Alrubaie S, Alsini R, AlZahrani S, Altowairqi S. Assessment of multiple sclerosis awareness: knowledge and attitude among saudi population in Taif City, KSA. Int J Adv Res 2016; 4: 1758-1766.
- 17) Michel L, Foucher Y, Vukusic S, Confavreux C, De Sèze J, Brassat D, Clanet M, Clavelou P, Ouallet J, Brochet B, Pelletier J, Labauge P, Lebrun C, Lepage E, Le Frere F, Jacq-Foucher M, Barriere P, Wiertlewski S, Laplaud D, Laplaud DA. Increased risk of multiple sclerosis relapse after in vitro fertilisation. J Neurol Neurosurg Psychiatry 2012; 83: 796-802.

- 18) Mainguy M, Tillaut H, Degremont A, Le Page E, Mainguy C, Duros S, Polard E, Leray E. Assessing the risk of relapse requiring corticosteroids after in vitro fertilization in women with multiple sclerosis. Neurology 2022; 99: e1916e1925.
- 19) Bhargava P, Fitzgerald KC, Calabresi PA, Mowry EM. Metabolic alterations in multiple sclerosis and the impact of vitamin D supplementation. JCI Insight 2017; 5: e95302.
- Menichini D, Forte G, Orrù B, Gullo G, Unfer V, Facchinetti F. The role of vitamin D in metabolic and reproductive disturbances of polycystic ovary syndrome: a narrative mini-review. Int J Vitam Nutr Res 2020; 92: 126-133.
- 21) Feige J, Moser T, Bieler L, Schwenker K, Hauer L, Sellner J. Vitamin D supplementation in multiple sclerosis: a critical analysis of potentials and threats. Nutrients 2020; 12: 783.
- 22) D'Anna R, Santamaria A, Giorgianni G, Vaiarelli A, Gullo G, Di Bari F, Benvenga S. Myo-inositol and melatonin in the menopausal transition. Gynecol Endocrinol 2017; 33: 279-282.
- 23) D'Anna R, Corrado F, Loddo S, Gullo G, Giunta L, Di Benedetto A. Myoinositol plus α-lactalbumin supplementation, insulin resistance and birth outcomes in women with gestational diabetes mellitus: a randomized, controlled study. Sci Rep 2021; 11: 1-5.
- 24) Laganà AS, Monti N, Fedeli V, Gullo G, Bizzarri M. Does Alpha-lipoic acid improve effects on polycystic ovary syndrome? Eur Rev Med Pharmacol Sci 2022; 26: 1241-1247.