



## University of Kut Journal

ISSN (E): 2616 - 7808 II ISSN (P): 2414 - 7419 www.kutcollegejournal.alkutcollege.edu.iq k.u.c.j.sci@alkutcollege.edu.iq



Special Issue for the Researches of the 6th Int. Sci. Conf. for Creativity for 16-17 April 2025

### The Prevalence of Fibromyalgia Among Women

Muhammad Mishal Khalaf 1, Arwa Adress Ahmed 2

#### **Abstract**

Introduction: Fibromyalgia is a rheumatic condition that causes muscle and bone pain as well as stiffness in the fibrous tendons that surround the joints. It is frequently accompanied by persistent weariness, mood swings, or sleep difficulties. However, it is not a dangerous or fatal disease, and the intensity of symptoms varies between individuals. Overall, women are more commonly affected by this condition than men. Methods: In this study, the research subjects consisted of women, including both expectant mothers and those who were not pregnant. The sample pool comprised 186 married women, 121 unmarried women, and 78 pregnant women, all of whom were infected with the illness. The study explored various themes, including age groups, sources of infection, and infection symptoms. Results: The study revealed that the largest age group infected with the disease consisted of married women aged 26-35 years, while single women between 15-25 years and pregnant women aged 26-35 years were also significantly affected. The primary causes of infection were identified as both psychological and pathological factors, with pain being the most prevalent symptom among infected women. Additionally, sleep issues, depression, and irritable bowel syndrome were found to be common symptoms experienced throughout the body.

**Keywords:** Disease, Fibromyalgia, Pregnant Women

# انتشار الألم العضلي الليفي بين النساء $^2$ عهد مشعل خلف $^1$ ، اروی ادریس احمد $^2$

#### لمستخلص

مقدمة: الألم العضلي الليفي هو حالة روماتيزمية تسبب آلم في العضلات والعظام بالإضافة إلى تصلب في الأوتار الليفية المحيطة بالمفاصل ، وغالبًا ما يصاحبها إرهاق مستمر أو تقلبات مزاجية أو صعوبات في النوم. ومع ذلك، فهو ليس مرضًا خطيرًا أو مميثًا، تختلف شدة الأعراض بين الأفراد . تتأثر النساء بهذه الحالة المرضية بشكل أكثر شيوعًا من الرجال. طريقة العمل : أجريت هذه الدراسة على الأمهات الحوامل والنساء غير الحوامل. وضمت مجموعة العينة 186 امرأة متزوجة و 121 امرأة غير متزوجة و 78 امرأة حامل، وجميعهن مصابات بالمرض. النتائج: كشفت الدراسة أن أكبر فئة عمرية مصابة بالمرض تكون بين النساء المتزوجات اللاتي تتراوح أعمار هن بين 16 و 25 عامًا، بينما تأثرت النساء العازبات اللاتي تتراوح أعمار هن بين 16 و 25 عامًا والنساء الحوامل اللاتي تتراوح أعمار هن بين 16 و 25 عامًا بشكل كبير. الاستنتاج: حُدِّدت الأسباب الرئيسية على والنساء الحوامل اللاتي تتراوح أعمار هن بين 16 و 25 عامًا بشكل كبير. الاستنتاج: حُدِّدت الأسباب الرئيسية على اضطرابات النوم والاكتناب ومتلازمة القولون العصبي من الاعراض الملازمة للمرض.

الكلمات المفتاحية: مرض، الألم العضلي الليفي، النساء الحوامل

#### **Affiliation of Authors**

- <sup>1,2</sup> College of Education for pure sciences, University of Mosul, Iraq, Mosul ,41001
- <sup>1</sup>education1443@gmail.com <sup>2</sup>arwabio2020@uomosul.edu.iq
- <sup>2</sup> Corresponding Author

Paper Info.
Published: Oct. 2025

ا**نتساب الباحثين** أ<sup>، 2</sup> كلية التربية للعلوم الصرفة، جامعة الموصل، العراق، الموصل، 41001

<sup>1</sup> education1443@gmail.com <sup>2</sup> arwabio2020@uomosul.edu.iq

2 المؤلف المراسل

معلومات البحث تأريخ النشر: تشرين الاول 2025

#### Introduction

Fibromyalgia is a chronic rheumatic condition [1] Chronic diseases are those that follow a person for a long time and have a direct impact on his or her overall health. Fibromyalgia is characterized by general pain in the body and hypersensitivity to stimuli, and is usually accompanied by fatigue, sleep disturbances, cognitive impairment, and depression. It is a biological marker that indicates alterations in the functional and chemical connections of the brain's pain processing system [2] According to [3], all of the symptoms that patients experience are absent from a visible organic lesion. Fibromyalgia symptoms can occur 5 years before diagnosis, and they are severe and impair all parts of life, particularly in young individuals (less than 39 years) or middle-aged (40-59 years) patients, as opposed to older patients (above 60 years). [4] The evident causes of the disease are related to the central and peripheral neurological systems, pain management, and changes in neuroendocrine organization [5] While there isn't a cure for severe pain, behavioral and cognitive therapy, exercises, and medicine are all employed in treatment. However, the treatments which frequently involve analgesics—only have temporary effects and do not cure the medical condition [6,7] The disease's prevalence varies according to the diagnostic standards applied [8]. However, the diagnostic approach utilized is determined by the clinical diagnosis symptoms. As a result, the patient may need to see multiple doctors before the disease is properly In 2016, diagnosed [9]. the International Association for the Study of Pain (IASP) coined the term "nociplastic pain" to describe the pain that occurs in fibromyalgia, which is mechanically distinct from other types of pain and neuropathic pain [10] The inhibition of pain signals in the central and peripheral nervous systems explains nociplastic pain, even though the underlying pathophysiology is not entirely known [11]. It was suggested in 1990 by the American College of Rheumatology (ACR) [12] Then, in 2010/2011, it was replaced with revised criteria that were based on symptoms [13,14]. These criteria were again updated in 2016 [15]. All of these guidelines were designed to streamline the diagnosis process by

establishing routine clinical evaluations in order to accurately identify the disease and provide proper therapy, including of these medications.(Duloxetine, Pregabalin, and Milnacipran) [16]. There is limited data on how fibromyalgia affects people in general, especially women. Pregnant women experience increased symptoms of the disease, particularly in the first and third trimesters, such as lower back and leg discomfort, persistent exhaustion, and stress. The adjustments could include One of the causes of infection in pregnant women is her body's hormones [17]. Pregnant women who acquire the disease have poorer pregnancy outcomes because of the disease's effects on both the mother and the fetuses and infants. Consequently, in order to support the mother and her fetus, the appropriate treatment measures needs to be taken. This study was carried out because, in spite of this, there is a dearth of research on the connection between this condition and pregnancy to find out how this illness affects pregnancy.

#### Methods

Samples: The current study concentrated on women in Iraq. The study included 186 married women affected with the disease, 121 single women, and 78 pregnant women ill with the condition. A total of 35 male-specific disorders were removed from the study because they were associated with female infections.

**Experimental design**: The study was conducted according to the following axes Age, Symptoms, Causes of injury, Other diseases accompanying the injury, Duration of injury, Injury treatment medications, Miscarriage, Birth of a stillborn baby, birth to a deformed child, Type of deformity. Statistical Analysis: The results were analyzed

statistically and the arithmetic mean was compared using the ANOVA program with a linear analysis of variance (Anova of variance) between the three groups under study at the 5% probability level.

#### **Results**

**Age**: The study found that the highest age group infected with the disease for married women was

between the ages of 26-35, followed by women between 15-25, while for single women, the ages between 15-25 were the highest, followed by the ages of 26-35, and for pregnant women it was between 26-35, followed by the age group 15-25. Table and Figure (1) indicate there are no statistical differences between the arithmetic means of the age groups investigated at the probability level of 0.05%.

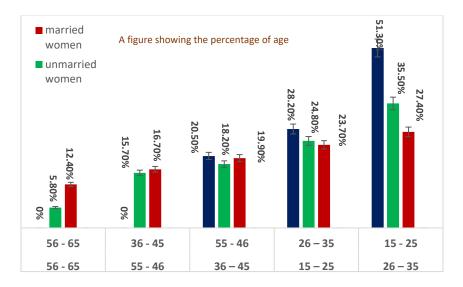


Figure (1) Age percentage for all groups

Signs and symptoms: Pain in all body regions, including migraine headaches, difficulty sleeping, depression, exhaustion, constant stress, and irritable bowel syndrome were observed in varying

degrees throughout the groups as shown in Figure (2). It appears that the arithmetic averages of the symptoms for the three groups differ in a way that is statistically significant.

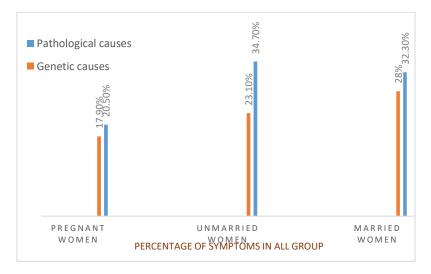


Figure (2) Percentage of symptoms among all groups

The causes of disease: The current study discovered that the reasons of disease were psychological, pathological, and genetic, and the

causes were the same for all three groups, as shown in Figure (3).

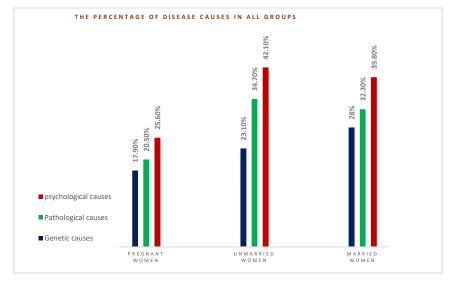


Figure (3) Percentage of causes of disease

**Duration of the disease**: According to Figure (4), the duration of infection with the disease varied, with married women with the highest percentage

(more than a month), while single and pregnant women had the highest percentage (less than three months).

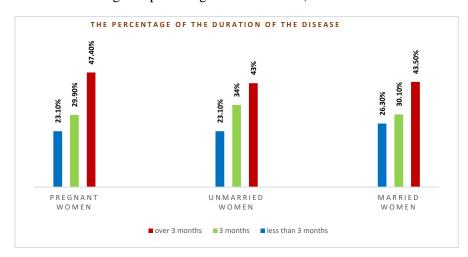


Figure (4) Percentage of infection duration

#### **Pharmaceutical**

The results of the study indicated that most of the infected women did not undergo specific treatment because no specific treatment has been discovered for the disease yet, but most of the medications that were prescribed are among the pain-relieving and sedative medications such as Panadol, Duloxetine, Cymbax, Flutac, Brufen, Lyrica,

Convitin, Effexor, and Cymplata, antibiotics, vitamins, and doctors also prescribed for pregnant patients to undergo physical and psychological rest and stay away from the causes of the disease. It is important to emphasize that the study's results indicate that the infected women also reported having multiple sclerosis, hypothyroidism, acute arthritis, and lupus in addition to fibromyalgia;

these claims have not been confirmed by medical or scientific research, this explanation may be due to fibromyalgia.

#### Study results for pregnant women

Miscarriage: The study observed that having

fibromyalgia associated with miscarriage, but not at large rates. The study showed that not having a miscarriage was the highest rate, and causing a miscarriage was the lowest rate. As shown in Figure (5).

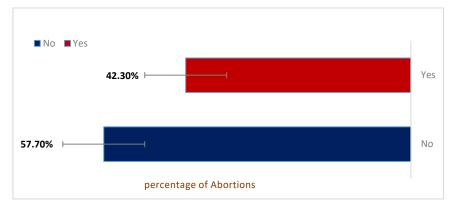


Figure (5) Percentage of miscarriage

Births: The study found that infection with the disease did not result in a significant percentage of stillbirths, but it did result in the birth of deformed newborns, including nervous system deformities, pulmonary hypoplasia, and skeletal system

deformities represented by spinal deformities, Down syndrome, and many pains that occur throughout the newborn's body without a clear deformity in figure (6).

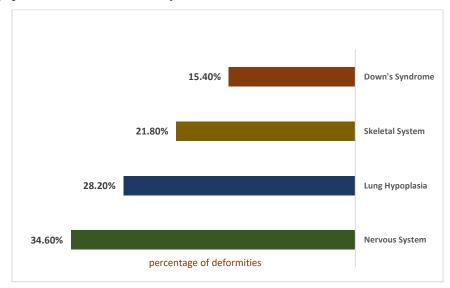


Figure (6) Percentage of deformities

#### **Discussion**

Fibromyalgia is a common syndrome, but it is often underestimated. Despite the risks involved, it is possible to lessen them if recognized early. This

syndrome is more prevalent in women, especially middle-aged women who are also of reproductive age [18]. This disease overlaps with other diseases in affected individuals, such as irritable bowel syndrome and temporomandibular joint

dysfunction and it is frequently accompanied by mental health issues, such as sleep difficulties and anxiety [19]. According to [20] this syndrome is defined by both tissue pain and physical pain that travels throughout the body due to an imbalance in the nervous system's pain pathways. Although there hasn't been enough research done on the subject, it's unknown whether fibromyalgia causes pregnancy problems or vice versa, some studies have linked the illness to problems during pregnancy, including spontaneous abortion and even breastfeeding difficulties [21]. Some studies supported our findings, such as one that found that fibromyalgia infection is accompanied by pain that causes physical disability, particularly pain in the lower back, leg, abdomen, and chest, as well as irritable bowel pain, headache, anxiety, depression, and dizziness [17]. According to research, patients are probably to be between the ages of 20- 64 [22]. Women, especially pregnant women, may have hormonal modifications as a result of these consequences. [23] Sleep disorders have been connected to the autonomic neuroendocrine system, which appears to be the root of the condition [24]. The high infection rates among pregnant women demonstrate the efficacy of placental neurohormones, as the placenta is an endocrine organ that produces a variety of cytokines, neuropeptides, and steroids [25]. In terms of psychological disorders, some studies show that having the disease causes anxiety and depression without explaining why [17], whereas one study suggests that these psychological disorders are caused by hypersensitivity to stimulation and its association with low pain values [26]. Studies confirm a reduction in pain during pregnancy and even after delivering [27]. Pregnancy is one of the times during which females experience numerous physiological and

biomechanical changes, and the symptoms of pregnancy are comparable to those of condition. This necessitates more clarity distinguishing between the usual signs of pregnancy and those of the disease. Muscle pain and indications of anxiety and sadness common during pregnancy. The symptoms of fibroids were the same, but anxiety and depression were more common in cases of the disease than in pregnancy without it [28,29]. These high rates of anxiety and depression resulted in fear of giving birth [30]. However, additional research suggests that similar psychological and physical symptoms may be passed on to the fetuses of pregnant women, resulting in alterations that could ultimately result in the fetuses' mortality [31,32]. Depression and anxiety may have long-term consequences if experienced before to pregnancy. [33] discuss newborn growth and the risk of developing psychological illnesses. The placenta is generally subjected to epigenetic dysregulation and serves as a transfer station for all materials to the fetus. As a result, the stress that affects mothers, such as anxiety and depression, will be transferred to the fetus and newborn in the future, and this needs dealing with these damages to pregnant women carefully [17]. The central nervous system undergoes alterations that are connected to the symptoms of fibromyalgia. It is important to comprehend the role of hormones, particularly sex hormones, in these symptoms and their various effects on pain receptors. Chronic motor pain is indicative of a disorder in the pain processing centers. Understanding the causes of persistent pain is essential. With the condition. In this respect, studies indicate a decrease in pain attacks through hormonal modulation of the pain pathways of adrenal gland, thyroid, and ovarian hormones [34], and another study indicates a relationship between pregnancy and the condition .This is related to estrogen levels, which are regarded as the cause of the condition [35], while a study of [36] indicated that there is not sufficient evidence to prove the relationship of estrogen with the disease, and that sleep disorders weaken pain activation pathways [37]. It leads to a feeling of fatigue and low energy, which leads to fatigue [38] and leads to the activation of inflammation [39]. When an injury occurs, significant amounts of stimulating neurotransmitters such as substance P will be twice as high in cerebrospinal fluid [40]. Glutamate with low levels of inhibitory neurotransmitters such serotonin as norepinephrine, and alterations in endogenous opioids in some parts of the brain which are chemicals implicated in pain regulation and dopamine release [41]. Norepinephrine level are high, while dopamine levels are low, which has been linked to health problems. Physical [42]. Fibromyalgia patients also have a decrease in the binding of receptors to drugs that relieve pain in some parts of the brain. With an increase in these chemicals, opioids produce excessive pain [43]. People with the disease suffer from cognitive difficulties such as trouble concentrating, poor memory, and problems with planning and decision-making, which are caused by weak interference between pain and cognitive processing in the brain [44]. In addition to changes in corticotrophin levels, increased secretion of adrenal hormone (ACTH), and decreased cortisol levels, individuals with the disease experience dysfunction in the hypothalamic-pituitary-adrenal axis, which in turn impacts the adaptive response [45]. Melatonin levels fall during the night, resulting in poor sleep quality, which in turn induces daily fatigue and increased pain perception [46]. A study recently discovered that the release

of melatonin 6\_Sulfatuxymelatonin (AMT6S) is found in substantial concentrations in patients with fibromyalgia. This explains the lack of melatonin release at night [47]. Numerous investigations of fibromyalgia have revealed an increase patients. oxidative stress levels in The accumulation of damaged mitochondrial DNA in cells causes elevated levels of tumor necrosis factors, which may contribute to the disease's etiology. The research of 80 women with the condition indicated that fibromyalgia decreased. In levels of thiols (antioxidant agents) accompanied by high levels of disulfide [48], there is also an association between genetic polymorphisms and disease in the serotonin A2 receptor region on chromosome 13 (which regulates the transfer of the catecholamine gene). These include dopamine D3 receptors and adrenaline receptors [49]. Chronic pain is common in patients for a variety of causes, including genetic variations Catcholamine O\_methyltransferase (COMT), resulting in high levels of catecholamines that cause pain via adrenergic receptors [50]. Fibromyalgia patients also have an imbalance of anti-cytokines. pro-Inflammation characterized by an increase in pro-inflammatory cytokines. This is caused by the activation of glial cells, which increases the production of proinflammatory cytokines [51,52], as discovered. Fibromyalgia is associated with reduced intestinal motility and increased bacterial growth in the small intestine, according to studies [53]. This bacterial alteration impacts intestinal permeability, raises tryptophan levels to generate indole, and impacts the central nervous system, resulting in a reduction in serotonin and melatonin synthesis [54]. Three genes—GBPI, TAARI, and GABRB3—were shown to differ statistically significantly in a research involving 496

fibromyalgia patients [55]. The role of TAARI is not totally established, but it is thought to be associated to dopamine action [56]. Interferons and cytokines typically induce GBPI, which is linked to symptoms of chronic pain syndromes such as irritable bowel syndrome [57]. Fibromyalgia is a disorder that produces abnormal pain signals. It is influenced by genetics, abnormal neuroendocrine activity, the nervous system, and environmental factors, and the pain that sufferers experience may be the result of an inability to process sensory inputs neurologically, as well as a deficiency in pain inhibition, which occurs due to impairment that affects small nerve fibers [58].

**Acknowledgment**: Supported by the Department of Biology, College of Education for Pure Sciences, Mosul University.

#### References

- [1] GG. Magtanong, AR. Spence, N .Czuzoj-Shulman and HA. Abenhaim. "Maternal and neonatal outcomes among pregnant women with fibromyalgia: a population-based,study,of,12,million,births"

  The Journal of Maternal-Fetal and Neonatal Medicine (32) 3. 2019.
- [2] T. Schmidt-Wilcke, and M. Diers. "New Insights into the Pathophysiology and Treatment of Fibromyalgia". *Biomedicines*, 5(2),22. 2017. https://doi.org/10.3390/biomedicines5020022.
- [3] R. Talotta, L. Bazzichi, M. Di Franco, R. Casale, A. Batticciotto, M. Gerardi, and P. Sarzi-Puttini. "One year in review 2017: fibromyalgia". *Clinical and experimental rheumatology*, 35 Suppl 105(3), 6–12. 2017.

- [4] J. Jiao, A. Vincent, S. Cha, C. Luedtke, and T. Oh. "Relation of age with symptom severity and quality of life in patients with fibromyalgia". *Mayo*Clinic proceedings, 89(2), 199–206. 2014. https://doi.org/10.1016/j.mayocp.2013.09.021.
- [5] K. Phillips, and D. Clauw, "Central pain mechanisms in chronic pain states--maybe it is all in their head". *Best practice & research. Clinical rheumatology*, 25(2), 141–154. 2011. https://doi.org/10.1016/j.berh.2011.02.005.
- [6] J. Painter, L. Crofford, J. Talbert . " Geographic variation of chronic opioid use in fibromyalgia". Clin Ther 2013;35:303-11. 10.1016/j. clinthera.02.003.2013.
- [7] D. Goldenberg. "Chronic Widespread Pain Lessons Learned from Fibromyalgia and Related Disorders". 1st ed. Vertical Health, LLC.2016
- [8] G. Jones, F. Atzeni, M. Beasley, E. Flüß, P. Sarzi-Puttini, and G. Macfarlane, G. "The prevalence of fibromyalgia in the general population: a comparison of the American College of Rheumatology 1990, 2010, and modified 2010 classification criteria". *Arthritis & rheumatology (Hoboken, N.J.)*, 67(2), 568–575.2016. https://doi.org/10.1002/art.38905.
- [9] E. Choy, S. Perrot, T. Leon, J. Kaplan, D. Petersel, A. Ginovker, and E. Kramer. "A patient survey of the impact of fibromyalgia and the journey to diagnosis". *BMC health services research*, *10*, 102. 2010 . https://doi.org/10.1186/1472-6963-10-102.
- [10] E. Kosek, M.Cohen, R. Baron, G. Gebhart, J. Mico, A. Rice, W. Rief, and A. Sluka, "Do we need a third mechanistic descriptor for

chronic pain states? ". Pain, 157(7),1382–1386.2016.

- [11] M. Fitzcharles, S. Cohen, D. Clauw, G. Littlejohn, C. Usui, and W. Häuser. "Nociplastic pain: towards an understanding of prevalent pain conditions". *Lancet (London, England)*, 397(10289), 2098–2110. 2021.https://doi.org/10.1016/S0140-6736(21)00392-5.
- [12] F. Wolfe, H. Smythe, M. Yunus, R. Bennett,
  C. Bombardier, D. Goldenberg, P. Tugwell,
  S. Campbell, M. Abeles, and P. Clark. "The American College of Rheumatology 1990
  Criteria for the Classification of Fibromyalgia.
  Report of the Multicenter Criteria Committee"
  Arthritis and rheumatism, 33(2), 160–172.1990.

https://doi.org/10.1002/art.1780330203.

[13] F. Wolfe, D. Clauw, M. Fitzcharles, D. Goldenberg, R. Katz, P. Mease, A. Russell, I. Russell, J. Winfield, and M. Yunus. "The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity". *Arthritis care & research*, 62(5), 600–610.2010.

https://doi.org/10.1002/acr.20140.

[14] F. Wolfe, D. Clauw, M. Fitzcharles, D. Goldenberg, W. Häuser, R. Katz, P. Mease, A. Russell, I. Russell, and J. Winfield. "Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR Preliminary Diagnostic Criteria for Fibromyalgia". The

Journal of rheumatology, 38(6), 1113–1122. 2011. https://doi.org/10.3899/jrheum.100594.

- [15] F. Wolfe, D. Clauw, M. Fitzcharles, D. Goldenberg, W. Häuser, R. Katz, P. Mease, A. Russell, I. Russell, and B. Walitt. "2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria". *Seminars in arthritis and rheumatism*, 46(3), 319–329.2016. https://doi.org/10.1016/j.semarthrit.2016.08.01 2.
- [16] G. Macfarlane, C. Kronisch, L. Dean, F. Atzeni, W. Häuser, E. Fluß, E. Choy, E. Kosek. "EULAR revised recommendations for the management of fibromyalgia". *Annals of the rheumatic diseases*, 76(2), 318–328.2017. https://doi.org/10.1136/annrheumdis-2016-209724.
- [17] H. Genç, M. Atasever, B. Duyur Çakit, M. Seval, and A. Koç. "The Effects of Fibromyalgia Syndrome on Physical Function and Psychological Status of Pregnant Females". *Archives of rheumatology*, 32(2), 129–140.

  2017.https://doi.org/10.5606/ArchRheumatol.2 017.6028
- [18] E. Guymer, G. Littlejohn, C. Brand, R. Kwiatek, "Fibromyalgia onset has a high impact on work ability in Australians". *Internal medicine journal*, 46(9), 1069–1074.2016. https://doi.org/10.1111/imj.13135
- [19] K. Kato PF. Sullivan, PNL. edersen NL. "Latent class analysis of functional somatic symptoms in a population-based sample of twins". J Psychosom Res ;68:447-53. 2010.

http://dx.doi.org/10.1016/j.jpsychores.2010.01. 010.

- [20] K. Sluka, and D. Clauw. "Neurobiology of fibromyalgia and chronic widespread pain". *Neuroscience*, *338*, 114–129.2016. https://doi.org/10.1016/j.neuroscience.2016.06
- [21] F. Wolfe, K. Ross, J. Anderson, I. Russell, and L. Hebert. "The prevalence and characteristics of fibromyalgia in the general population". *Arthritis and rheumatism*, *38*(1), 19–28. 1995. https://doi.org/10.1002/art.1780380104
- [22] M. Topbas, H. Cakirbay, H. Gulec, E. Akgol, I. and G. Can. "The prevalence of fibromyalgia in women aged 20-64 in Turkey". *Scandinavian journal of rheumatology*, 34(2), 140–144.2005.
- [23] D. Casagrande, Z. Gugala, S. Clark, and R. Lindsey. "Low Back Pain and Pelvic Girdle Pain in Pregnancy". *The Journal of the American Academy of Orthopaedic Surgeons*, 23(9), 539–549. 2015. https://doi.org/10.5435/JAAOS-D-14-00248
- [24] F. Jahan, K. Nanji, W. Qidwai, and R. Qasim. "Fibromyalgia syndrome: an overview of pathophysiology, diagnosis and management". *Oman medical journal*, 27(3), 192–195.2012. https://doi.org/10.5001/omj.2012.44
- [25] M. Bonis, M. Torricelli, F. Severi, S. Luisi, V. De Leo, and F. Petraglia. "Neuroendocrine aspects of placenta and pregnancy ". Gynecological endocrinology: the official journal of the International Society of Gynecological Endocrinology, 28 Suppl 1, 22—

- 26. 2012. https://doi.org/10.3109/09513590.2012.65193
- [26] J. Marinus, and J. Van Hilten. "Clinical expression profiles of complex regional pain syndrome, fibromyalgia and a-specific repetitive strain injury: more common denominators than pain? ". Disability and rehabilitation, 28(6), 351–362.2006. https://doi.org/10.1080/09638280500287320
- [27] I. Ohel, A. Walfisch, D. Shitenberg, E. Sheiner, and M. Hallak. "A rise in pain threshold during labor: a prospective clinical trial. *Pain*", *132Suppl1*,S104–S108. 2007. https://doi.org/10.1016/j.pain.2007.05.007
- [28] M. Uçar, U. Sarp, O. Karaaslan, A. Gül, N. Tanik, and H. Arik. "Health anxiety and depression in patients with fibromyalgia syndrome". *The Journal of international medical research*, 43(5), 679–685.2015. . https://doi.org/10.1177/0300060515587578
- [29] U. Sener, K. Ucok, A. Ulasli, A. Genc, H. Karabacak, N. Coban, H. Simsek, and H. Cevik, H. "Evaluation of health-related physical fitness parameters and association analysis with depression, anxiety, and quality of life in patients with fibromyalgia". *International journal of rheumatic diseases*, 19(8), 763–772.2016. https://doi.org/10.1111/1756-185X.12237
- [30] H. Storksen, M. Eberhard-Gran, S. Garthus-Niegel, and A. Eskild. "Fear of childbirth; the relation to anxiety and depression". *Acta obstetricia et gynecologica Scandinavica*, 91(2), 237–242.2012.

8.

https://doi.org/10.1111/j.1600-0412.2011.01323.x.

- [31] C. Urech, N. Fink, N. I. Hoesli, F. Wilhelm, J. Bitzer, and J. Alder, "Effects of relaxation on psychobiological wellbeing during pregnancy: a randomized controlled trial". *Psychoneuroendocrinology*, *35*(9), 1348–1355.2010. https://doi.org/10.1016/j.psyneuen.2010.03.00
- [32] A. Schitter, M. Nedeljkovic, H. Baur, J. Fleckenstein, and L. Raio, "Effects of Passive Hydrotherapy WATSU (WaterShiatsu) in the Third Trimester of Pregnancy: Results of a Controlled Pilot Study". *Evidence-based complementary and alternative medicine : eCAM*, 2015, 437650. https://doi.org/10.1155/2015/437650.
- [33] C. Monk, J. Spicer, and F. Champagne. "Linking prenatal maternal adversity to developmental outcomes in infants: the role of epigenetic pathways". *Development and psychopathology*, 24(4), 1361–1376.2012. https://doi.org/10.1017/S0954579412000764.
- [34] N. Fayed, E. Andres, G. Rojas, S. Moreno, A. Serrano-Blanco, M. Roca, and J. Garcia-Campayo. "Brain dysfunction in fibromyalgia and somatization disorder using proton magnetic resonance spectroscopy: a controlled study". *Acta psychiatrica Scandinavica*, 126(2), 115–125.2012. https://doi.org/10.1111/j.1600-0447.2011.01820.x
- [35] B. Leblebici N. Turhan M. Adam N. Çetin S. Bagis. "Fibromyalgia Syndrome in Geriartric population". Turk J Rheumatol;24:6-9.2009.

- [36] O. Altındag. "Neuroendrocrinologic disfunctions in Fibromyalgia". Turk J Rheumatol ;24:98-102.2009.
- [37] E. Choy "The role of sleep in pain and fibromyalgia". *Nature*reviews.Rheumatology, 11(9),513–520.2015.

  https://doi.org/10.1038/nrrheum.2015.56
- [38] Y. Wu, L. Chang, H. Lee, S. Fang, and P. Tsai, "Sleep disturbances in fibromyalgia: A meta-analysis of case-control studies". *Journal of psychosomatic research*, 96,89–97. 2017. https://doi.org/10.1016/j.jpsychores.2017.03.0 11.
- [39] L. Palagini, C. Carmassi, C. Conversano, C. Gesi, L. Bazzichi, C. Giacomelli, and L. Dell'Osso. "Transdiagnostic factors across fibromyalgia and mental disorders: sleep disturbances may play a key role. A clinical review". *Clinical and experimental rheumatology*, *34*(2 Suppl 96), S140–S144.2016.
- [40] I. Russell, M. Orr, B. Littman, G. Vipraio, D. Alboukrek, J. Michalek, Y. Lopez, and F. MacKillip. "Elevated cerebrospinal fluid levels of substance P in patients with the fibromyalgia syndrome". *Arthritis and rheumatism*, *37*(11), 1593–1601.1994. https://doi.org/10.1002/art.1780371106
- [41] R. Staud, and M. Spaeth. "Psychophysical and neurochemical abnormalities of pain processing in fibromyalgia".. *CNS spectrums*, *13*(3Suppl5),12–17. 2008. https://doi.org/10.1017/s109285290002678x.
- [42] A. Rus, F. Molina, M. Del Moral, M. Ramírez-Expósito, and j. Martínez-Martos.
  "Catecholamine and Indolamine Pathway: A

Case-Control Study in Fibromyalgia". *Biological research fornursing*, 20(5),577–586.2018. https://doi.org/10.1177/1099800418787672

- [43] L. Watkins, M. Hutchinson, K. Rice, and S. Maier. "The "toll" of opioid-induced glial activation: improving the clinical efficacy of opioids by targeting glia". *Trends in pharmacological sciences*, *30*(11), 581–591.2009. https://doi.org/10.1016/j.tips.2009.08.002.
- [44] C. Galvez-Sánchez, C. Muñoz Ladrón de Guevara, C. Montoro, M. Fernández-Serrano, S. Duschek, and G. Reyes Del Paso. "Cognitive deficits in fibromyalgia syndrome are associated with pain responses to low intensity pressure stimulation". *PloS one*, *13*(8), e0201488.2018. https://doi.org/10.1371/journal.pone.0201488
- [45] E. Griep, J. Boersma, and E. Kloet. "Altered reactivity of the hypothalamic-pituitary-adrenal axis in the primary fibromyalgia syndrome". *The Journal of rheumatology*, 20(3), 469–474.1993.
- [46] j. Wikner, u. Hirsch, l. Wetterberg, and S. Röjdmark. "Fibromyalgia--a syndrome associated with decreased nocturnal melatonin secretion". *Clinical endocrinology*, 49(2), 179–183.1998. https://doi.org/10.1046/j.1365-2265.1998.00503.x
- [47] W. Caumo, M. Hidalgo, A. Souza, I. Torres, and Antunes, "Melatonin is a biomarker of circadian dysregulation and is correlated with major depression and fibromyalgia symptom severity". *Journalofpainresearch*, *12*,545–556. 2019.https://doi.org/10.2147/JPR.S176857.

- [48] A. Tuzcu, R. Baykara, M. Alışık, A. Omma, G. Acet, E. Dogan, M. Cure, F. Duygun, E. Cure, and O. Erel, O. "Alteration of Thiol-Disulfide Homeostasis in Fibromyalgia Syndrome". *Acta medica* (*HradecKralove*), 62(1),12–18.2019. https://doi.org/10.14712/18059694.2019.40.
- [49] L. Arnold, J. Hudson, E. Hess, A. Ware, A. Fritz, M. Auchenbach, *et al.* "Family study of fibromyalgia. Arthritis Rheum".;50:94452.2004.
- [50] A. Brenton, C. Lee, S. Kabaria, M. Hafez, S. Kantorovich, B. Meshkin. "Association of catechol-o-methyltransferase single nucleotide polymorphisms. Ethnicity, and sex in a large cohort of fibromyalgia patients". J Pain.;18:S75.2017.
- [51] D. Malhotra, A. Saxena, S. Dar, V. Kumar, N. Nasare, A. Tripathi, et al. "Evaluation of cytokine levels in fibromyalgia syndrome patients and its relationship to the severity of chronic pain. J Musculoskelet Pain";20:164–9.2012.
- [52] D. Mendieta, D. Cruz-Aguilera, M. Barrera-Villalpando, E. Becerril-Villanueva, R. Arreola, E. Hernández-Ferreira, S. Pérez-Tapia, G. Pérez-M. Garcés-Alvarez, L. Aguirre-Cruz, M. Velasco-Velázquez, and 1. Pavón, L. "IL-8 and IL-6 primarily mediate the inflammatory response in fibromyalgia patients". *Journaofneuroimmunology*, 290,22–25. 2016. https://doi.org/10.1016/j.jneuroim.2015.11.011
- [53] D. Wallace, and D. Hallegua. "Fibromyalgia: the gastrointestinal link". *Current pain and*

*headache reports*, 8(5), 364–368.2004. https://doi.org/10.1007/s11916-996-0009-z.

- [54] D. García Rodríguez, and C. Abud Mendoza. "Physiopathology of fibromyalgia. Fisiopatología de la fibromialgia". *Reumatologia clinica*, 16(3), 191–194. 2020. https://doi.org/10.1016/j.reuma.2020.02.003.
- [55] B. Oertel, and J. Lötsch. "Genetic mutations that prevent pain: implications for future pain medication". *Pharmacogenomics*, 9(2), 179–194.2008.

https://doi.org/10.2217/14622416.9.2.179.

[56] L. Lindemann, C. Meyer, K. Jeanneau, A. Bradaia, L. Ozmen, H. Bluethmann, B. Bettler,
B. "Trace amine-associated receptor 1 modulates dopaminergic activity". The Journal of pharmacology and experimental

*therapeutics*, *324*(3), 948–956.2008. https://doi.org/10.1124/jpet.107.132647.

[57] M. Buhr, M. Mähler, R. Geffers, W. Hansen, A. Westendorf, J. Lauber, J. Buer, B. Schlegelberger, H. Hedrich, and A. Bleich. "Cd14, Gbp1, and Pla2g2a: three major candidate genes for experimental IBD identified by combining QTL and microarray analyses". *Physiological genomics*, 25(3), 426–434.2006.

https://doi.org/10.1152/physiolgenomics.0002 2.2005.

[58] M. Gyorfi, A. Rupp, and A. Abd-Elsayed, A. (2022). "Fibromyalgia Pathophysiology". *Biomedicines*, 10(12),3070. 2022.

https://doi.org/10.3390/biomedicines10123070.