The occurrence of autoimmune diseases among women and the role of regular exercise in improving health

Oruba k. Albermani[1], Mays alreem A. Aljebory[2],Eklas M.Al-sharifi[3]

[1,3]Department of biology, College of science for women, University of Babylon, Iraq

[2] Department: Medical Laboratories Techniques , College of Health and Medical Techniques , Al-Mustaqbal University , Iraq

Key words Autoimmune disease ,women, exercise training.

Abstract

Autoimmune diseases are conditions characterized by immune dysregulations leading to tissue damage in the host. Autoimmune disease rates are increasing rapidly in many parts of the world due to environmental and lifestyle factors. Most autoimmune diseases require lifelong treatment and significantly impact affected individuals and their families, society, and healthcare costs. There are more than 80 types of AID, including common pathologies such as type 1 diabetes, systemic lupus erythematous (SLE), multiple sclerosis (MS), and rheumatoid arthritis (RA) as well as rarer diseases that may take years to diagnose. Exercise has a significant impact on improving the quality of life for women living with autoimmune diseases. Regular physical activity helps reduce systemic inflammation, regulate immune function, and alleviate symptoms such as pain, stiffness, and fatigue—common challenges associated with these conditions. Beyond physical benefits, exercise enhances mental well-being by reducing stress and anxiety, which can exacerbate autoimmune flares. Activities

such as yoga, swimming, and walking are particularly beneficial, as they combine low-impact movement with stress-relief techniques. Tailored exercise regimens not only help women better manage their symptoms but also foster a sense of empowerment and control over their health. By integrating exercise into daily routines, women with autoimmune diseases can achieve improved physical and emotional resilience, ultimately leading to a higher quality of life.

The aim of this review is to highlight the Occurrence of autoimmune diseases among women and summarize the role of regular exercise training in decrease the symptoms or healing of these disorder conditions.

This paper reviews the existing research on sustainability and sustainable development around the world cares with health of women

الملخص

الأمراض المناعية الذاتية هي حالات تتميز باضطرابات المناعة التي تؤدي إلى تلف الأنسجة في الجسم. تتزايد معدلات الإصابة بالأمراض المناعية الذاتية بسرعة في العديد من أنحاء العالم بسبب العوامل البيئية ونمط الحياة. تتطلب معظم الأمراض المناعية الذاتية علاجًا مدى الحياة وتؤثر بشكل كبير على الأفراد المصابين وأسرهم والمجتمع وتكاليف الرعاية الصحية. هناك أكثر من ٨٠ نوعًا من الأمراض المناعية الذاتية، بما في ذلك الأمراض الشائعة مثل مرض السكري من النوع الأول، (RA) ، والتهاب المفاصل الروماتويدي(MS) ، والتصلب المتعدد(SLE) والذئبة الحمامية الجهازية بالإضافة إلى الأمراض النادرة التي قد يستغرق تشخيصها سنوات. للتمارين الرياضية تأثير كبير على تحسين نوعية الحياة للنساء المصابات بأمراض المناعة الذاتية. يساعد النشاط البدني المنتظم في تقليل الالتهابات الجهازية، وتنظيم وظائف المناعة، وتخفيف الأعراض مثل الألم، والتصلب، والتعب – التحديات الشائعة المرتبطة بهذه الحالات. بالإضافة إلى الفوائد الجسدية، تعمل التمارين الرياضية على تعزيز الصحة العقلية من خلال تقليل التوتر والقلق، مما قد يؤدي إلى تفاقم نوبات المناعة الذاتية. تعتبر الأنشطة مثل اليوجا والسباحة والمشي مفيدة بشكل خاص، حيث تجمع بين الحركة منخفضة التأثير وتقنيات تخفيف التوتر. لا تساعد أنظمة التمارين المصممة خصيصًا النساء على إدارة أعراضهن بشكل أفضل فحسب، بل تعزز أيضًا الشعور بالتمكين والسيطرة على صحتهن. من خلال دمج التمارين في الروتين اليومي، يمكن للنساء المصابات بأمراض المناعة الذاتية تحقيق مرونة بدنية وعاطفية محسنة، مما يؤدي في النهاية إلى جودة حياة أعلى. يهدف هذا الاستعراض إلى تسليط الضوء على حدوث أمراض المناعة الذاتية بين النساء وتلخيص دور التدريب المنتظم على التمارين الرياضية في تقليل أعراض أو علاج حالات الاضطراب هذه.

تستعرض هذه الورقة البحثية الأبحاث الحالية حول الاستدامة والتنمية المستدامة في جميع أنحاء العالم التي تهتم بصحة المرأة

1.Introduction

1.1Autoimmune disease (concept and types)

Autoimmune diseases are conditions characterized by immune dysregulation leading to tissue damage in the host. Autoimmune disease rates are increasing rapidly in many parts of the world due to environmental and lifestyle factors(Conrad. *e tal.,*2023). Most autoimmune diseases require lifelong treatment and significantly impact affected individuals and their families, society, and healthcare costs.(Miller. *e tal.,*2023). There are more than 80 types of AID, including common pathologies such as type 1 diabetes, systemic lupus erythematosus (SLE), multiple sclerosis (MS), and rheumatoid arthritis (RA) as well as rarer diseases that may take years to diagnose(Dinse . *e tal.,* 2020) Various factors contribute to this disparity, including biological, hormonal, and environmental influences. Understanding these factors is crucial for addressing the unique health challenges faced by women with autoimmune diseases. .

1.2 Occurrence of Autoimmune disease

The occurrence of autoimmune diseases in women is significantly higher than in men, with estimates suggesting that women account for approximately 78% of those affected in the United States(Wang, 2022). For many individual autoimmune conditions, there is a higher female-to-male ratio, e.g. systemic lupus erythematosus (SLE) 7:1, Sjogren's syndrome 9:1, and rheumatoid arthritis or

systemic sclerosis 3:1 (Smith Bouvie. *e tal.,* 2008)(Van Den Hoogen. *e tal.,*2013). Women undergo various hormonal changes throughout their life: during puberty, pregnancy, and then in menopause(Desai , Brinton .2019). These endocrine transitions in women may increase their susceptibility to autoimmune conditions, and many autoimmune conditions such as SLE, systemic sclerosis, rheumatoid arthritis, and psoriasis develop during the female reproductive age infuenced by the T cell cytokine-mediated response and hormonal, immunological, and bodily changes(. De Carolis. *e tal.,*2019). There are over 100 types of autoimmune diseases that predominantly affect women. Approximately 80% of all patients diagnosed with autoimmune diseases are women (Invernizzi . *e tal.,*2009) . The prevalence of autoimmune diseases in women is significantly higher than in men, with estimates indicating that women account for approximately 75-80% of those affected by these conditions (Shukla et al., 2024) (Goulmamine. *e*

tal., 2024). Autoimmune diseases affect up to 75% of women, with over 80 different types identified, including lupus, rheumatoid arthritis, and multiple sclerosis(Shukla et al., 2024). The prevalence ratio is approximately 2:1, indicating that women are twice as likely to develop autoimmune disorders compared to men(Angum et al., 2020).

1.2.1 Sex chromosomes

Men and women alike are born with 23 pairs of chromosomes, with 22 pairs of autosomes and one pair of sex chromosomes, the differentiating factor between the two genders. Women have XX sex chromosomes, while men have XY sex chromosomes. The X and Y sex chromosomes vary greatly in size as the X chromosome is physically larger than the Y chromosome. This disproportion between the two chromosomes suggests that the X chromosome contains more genes than the Y chromosome (Smith-Bouvier .*e tal.,*2008).The X chromosomes contain approximately 800-900 genes coded to provide instructions for proteins, entailing for 5% of total DNA in human cells, whereas, the Y chromosomes contain approximately 50-60 genes coded to provide instructions for proteins and this entails about 2% of total DNA in human cells(Carrel , Willard .2005)(Willard .2003) . Furthermore, the X chromosome also stains for a greater amount of immune-related genes as well as immune egulatory genes, which aids and induces immunological responses in the body (Schurz . *e tal.,*2019).

1.2.2 Rheumatoid arthritis and Sjogren's syndrome

Autoimmune conditions such as rheumatoid arthritis and Sjogren's syndrome are hypothesized to occur more in women due to the hormonal changes women experience. Rheumatoid arthritis is characterized by painful, swollen, stiff joints, often accompanied by fever, fatigue, and weightless. It causes chronic inflammation of various joints due to the synovium of the joints being compromised. Typically, the synovium, which is soft tissue lining the joints and tendons, aids with movement, cartilage and bone of the affected joint. It is hypothesized that women between the ages of 40 and 60 are more likely to develop rheumatoid arthritis compared to men, due to undergoing hormonal changes during menopause. Menopause decreases estrogen and progesterone levels, which is thought to serve as a protective mechanism for bones and joints(Roman. *e tal.,*2016).Estrogen in larger quantities can decrease inflammation by increasing regulatory cytokines such as interleukin-10 (IL-10) and transforming growth factor-β (TGFB), which is why it is believed to act as a protective mechanism against rheumatoid arthritis and Sjogren's syndrome(Brandt . *e tal.,*2015) .

Rheumatoid arthritis swelling and inflammation of the joints

1.2.3 Psoriasis

Psoriasis is an autoimmune disorder characterized by the increased thickness of the stratum corneum layer. This hyperkeratosis leads to the formation of red, salmon, and white-colored scaly, itchy plaques. These plaques can occur anywhere on the skin but predominantly seen on the back, elbows, knees, and scalp. This debilitating disorder can often cause a great deal of physical, mental, and emotional stress upon those diagnosed. With a prevalence of 11% in Caucasian and Scandinavian populations, psoriasis is generally impacted 2% of the global population. However, in African and Asian populations, less than 1% of individuals are affected. Often triggers such as trauma, stress, colder climates, smoking, alcohol, and infections can increase flare-

up frequency as well as worsen the symptoms (Rendon , Schäkel .2019) . Typically, the severity of psoriasis is indicated via the psoriasis area severity index (PASI) scale, which involves the areas affected as well as the severity of the area affected upon. Women tend to have lower PASI scores in comparison to men. Despite more women being affected by psoriasis, they do not suffer from severe symptoms (Hägg . *e tal.,*2017) . It is unclear as to why men suffer from more severe symptoms of psoriasis. Furthermore, current research has uncovered that hormonal changes often plays a significant role in triggering the onset of psoriasis for many who are predisposed to it genetically or may cause flare-ups of those already diagnosed. This is because the skin is affected directly by the endocrine system and severely impacted by the hormonal changes of sex hormones, prolactin, glucocorticoids, epinephrine, thyroid hormone, and insulin, which are seen in greater quantity or solely in women (Roman. *e tal.,*2016). Women typically experience more hormonal changes than men, as well as often contain greater quantities of many of the hormones which directly act as triggers for psoriasis, lending to a potential theory as to why more women are likely to developed psoriasis than men.

1.2.4Multiple sclerosis

(MS) is a chronic, immune-mediated, inflammatory, demyelinating disease of the central nervous system (Hauser . *e tal.,*2006), with a female-to-male incidence rate ratio of 3:1 (Wallin . *e ta.,*2012). Since MS is typically diagnosed in young adulthood (Sanai . *e*

*tal.,*2012), a majority of women living with MS will undergo menopause after MS diagnosis. However, rates of late-onset MS have also increased, particularly among women (Koch-Henriksen. *e tal.,*2018). Further, since the advent of disease-modifying therapies (DMTs) to treat MS, the life expectancy and median age of patients living with MS has increased , thereby necessitating awareness among clinicians of the changing needs associated with older patients. For both women and men, increasing age is associated with changes in the MS course, notably a switch from a predominantly relapsing-remitting course to progressive phenotypes with greater disability accumulation (Musella. *e tal.,*2018). The symptoms of MS in older patients may be further impacted not only from the effects of somatic aging but also from the effects of other neurodegenerative diseases that are typical in older age (Sanai. *e tal.,*2016). In addition, the onset of menopause in women presents further challenges for the management of MS since some symptoms experienced during this life transition, such as cognitive impairment, depression and anxiety, sleep disturbance and fatigue, and bladder impairment, can overlap with those of MS (Bove. *e tal.,*2016).

1.2.5 systemic scleroderma

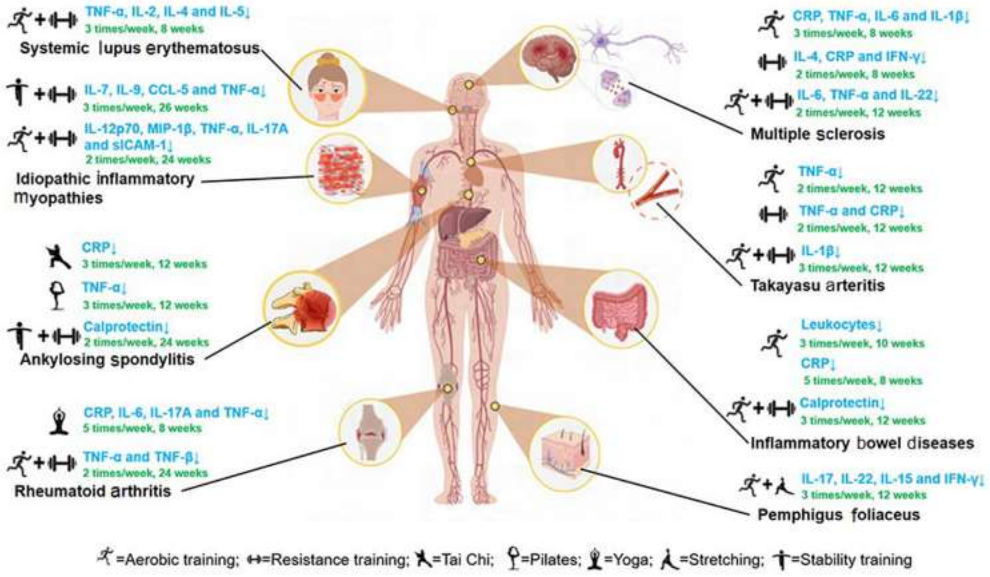
Systemic sclerosis (SSc) is a complex autoimmune rheumatic disease that is characterized by widespread skin (scleroderma) and internal organ fibrosis, immune system dysregulation, and vascular alterations.SSc is a rare rheumatological condition (prevalence: ~20 per million) and is more common in females than males (~7:1)The excess collagen seen in SScl is triggered by inflammation, which appears to simulate the cells in the body that make collagen. While the results of this process are most easily seen in the skin ("scleroderma" is literally translated "hard skin"), many other parts of the body can become involved. When this takes place, life-threatening complications may ensue (Hughes *e tal.,* 2020)

A woman with scleroderma may experience some of their fingers falling off spontaneously due to the lack of adequate nutrition as a result of the increased secretion of skin proteins such as collagen.

2. Influence of exercise training on autoimmune disease(AID)

Exercise training is recommended for patients with autoimmune disease in combination with medication and clinical care to improve quality of life, cardiorespiratory capacity, and muscle strength, and to alleviate symptoms such as pain and depression.(Sharif. *e tal.,*2018)(Edwards. *e tal.,*2022) Inflammation palliation is an important goal in the treatment of autoimmune diseases. All autoimmune diseases share common features, including elevated circulating inflammatory markers such as interleukin (IL)-6, tumor necrosis factor a (TNF-a), and C-reactive protein (CRP) under basal or resting conditions.(Ploeger. *e tal.,*2009) Regular exercise training has been linked in numerous studies with an anti-inflammatory effect.(Gleeson. *e tal.,*2011) Possible mechanisms of the anti-inflammatory effects of exercise include increased release of hormones (cortisol and adrenaline) and myokines that downregulate the production of proinflammatory cytokines by immune cells. Exercise training also mobilizes regulatory T (Treg) cells, natural killer cells, and other immune cells that release the anti-inflammatory cytokine IL-10. Exercise training is typically associated with decreased visceral adipose tissue volume. This is important because an increase in visceral adipose tissue caused by physical inactivity and overeating leads to an expansion of resident inflammatory innate and adaptive immune cells that undergird systemic inflammation.(Valenzuela. *e tal.,2023)* Taken together, exercise training is important for overall immune health through its effects on immune cell recruitment and enhanced surveillance,

antimicrobial activities, and reduced systemic inflammation(Nieman , Sakaguchi . 2022)



2.1 Yoga and its impact on autoimmune disease

Yoga is a profound science of a mind–body technique that acts via a well–defined psycho–neuro–endocrine pathway, aims to rejuvenate mind by counteracting the stress response, restores endocrine health and relaxes the body by maintaining flexibility and improving joint mobility. Majority of complex diseases like cardiovascular diseases, depression, cancers, and autoimmune diseases arising due to interaction of several genes and environmental factors and our unhealthy social habits have common underlying etiology like persistent activation of the hypothalamic–pituitary–adrenal axis, oxidative stress (OS), depression, anxiety, stress, shorter telomeres, chronic inflammation, gut microbiome

dysbiosis and dysregulated immune system. Yoga targets each of these factors and corrects the dysregulated systems and brings about homeostasis. Hence, it can be used as an adjunct therapy in the management of these disorders. Adoption of a simple lifestyle-based intervention like ga and meditation may help to break the surge of triggering factors as it reduces inflammatory state by regulating OS induced cellular damage, maintains cortisol melatonin rhythms, elevates endorphin levels and maintains a balance of pro-inflammatory and anti-inflammatory cytokines. It also normalizes the levels of dysregulated transcripts, especially of genes regulating free radical levels and maintaining DNA integrity(Dhawan. *e tal.,*2018)(Gautam. *e tal.,* 2018) Yoga also aids in reducing the rate of cellular aging by upregulation of telomerase enzyme activity and genes responsible for DNA repair and cell-cycle control. Yoga improves mitochondrial integrity by altering the expression levels of transcripts which maintain mitochondrial integrity (AMPK, IGF1R, PRC-1, TFAM, SIRT-1, TIMP-1, and CLOTHO) which aids in the maintenance of optimal free radical levels, improves energy and insulin metabolism and thus reduces the rate of telomere attrition by supra-physiological ROS levels (Tolahunase. *e tal.,* 2017)

(Tolahunase. *e tal.,*2018) .

3. Conclusion

Autoimmune diseases disproportionately affect women, posing significant challenges to their physical and emotional well-being. While these conditions often require medical intervention, evidence

suggests that lifestyle modifications, including a balanced diet, stress management, and regular physical activity, play a crucial role in improving outcomes. Exercise, in particular, has been shown to reduce inflammation, enhance immune regulation, and alleviate fatigue—key symptoms associated with autoimmune disorders. Furthermore, adopting a holistic lifestyle that prioritizes mental health and resilience can complement medical treatments, fostering better overall health and quality of life.

5. Reference :

- Angum, F., Khan, T., Kaler, J., Siddiqui, L., & Hussain, A. (2020). The Prevalence of Autoimmune Disorders in Women: A Narrative Review. *Cureus*, *12*(5).
- Bove R, Vaughan T, Chitnis T, Wicks P, De Jager PL.(2016) Women's experiences of menopause in an online MS cohort: a case series. *Mult Scler Relat Disord.* 9:56–9.
- Brandt JE, Priori R, Valesini G, Fairweather D.(2015) Sex differences in Sjögren's syndrome: a comprehensive review of immune mechanisms. Biol Sex Differ., 6:19.
- Carrel L, Willard HF(2005) X-inactivation profile reveals extensive variability in X-linked gene expression in females. Nature. 434:400-404. 10.1038/nature03479
- Conrad N, Misra S, Verbakel JY, et al.(2023) Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: A population-based cohort study of 22 million individuals in the UK. The Lancet ,401:1878–90.

- De Carolis S, Moresi S, Rizzo F, Monteleone G, Tabacco S, Salvi S, et al.(2019) Autoimmunity in obstetrics and autoimmune diseases in pregnancy. Best Pract Res Clin Obstet Gynaecol. 60:66–76.
- Desai MK, Brinton RD.(2019) Autoimmune disease in women: endocrine transition and risk across the lifespan. Front Endocrinol. ;10:265. 12.
- Dinse GE, Parks CG, Weinberg CR,(2020) et al. Increasing prevalence of antinuclear antibodies in the United States. Arthritis Rheumatol.;72(6):1026–1035.
- Edwards T, Michelsen AS, Fakolade AO, Dalgas U, Pilutti LA.(2022) Exercise training improves participation in persons with multiple sclerosis: A systematic review and meta-analysis. J Sport Health Sci ;11:393– 402
- Female predominance and X chromosome defects in autoimmune diseases. Invernizzi P, Pasini S, Selmi C, Gershwin ME, Podda M.(2009) J Autoimmun.;33:12–16.
- Gleeson M, Bishop NC, Stensel DJ, Lindley MR, Mastana SS, Nimmo MA.(2011) The anti-inflammatory effects of exercise: Mechanisms and implications for the prevention and treatment of disease. Nat Rev Immunol;11:607–15.
- Hägg D, Sundström A, Eriksson M, Schmitt-Egenolf M(2017) Severity of psoriasis differs between men and women: a study of the clinical outcome measure Psoriasis Area and Severity Index (PASI) in 5438 Swedish register patients. Am J Clin Dermatol. 18:583–590. 10.1007/s40257-017-0274-0

- Hauser SL, Oksenberg JR. (2006) The neurobiology of multiple sclerosis: genes, inflammation, and neurodegeneration. *Neuron.* 52:61–76.
- Hughes M.,Allanore Y., Denton C.P., Matucci-Cerinic M.(2020).Systemic Sclerosis. EMJ Rheumatol. 7[1]:100-109.
- Koch-Henriksen N, Thygesen LC, Stenager E, Laursen B, Magyari M.(2018) Incidence of MS has increased markedly over six decades in Denmark particularly with late onset and in women. *Neurology.* 90:e1954–63.
- M Tolahunase; R Sagar; R Dada.(2017) Impact of Yoga and Meditation on Cellular Aging in Apparently Healthy Individuals: A Prospective, Open-Label Single-Arm Exploratory Study. Oxid Med Cell Longev 2017, 7928981
- Miller FW.(2023) The increasing prevalence of autoimmunity and autoimmune diseases: An urgent call to action for improved understanding, diagnosis, treatment, and prevention. Curr Opin Immunol ;80:102266.
- MR Tolahunase; R Sagar; M Faiq; R Dada.(2018) Yoga- and meditation-based lifestyle intervention increases neuroplasticity and reduces severity of major depressive disorder: A randomized controlled trial. Restor Neurol Neurosci 36, 423-442
- *Musella A*, Gentile A, Rizzo FR, De Vito F, Fresegna D, Bullitta S, et al.(2018) Interplay between age and neuroinflammation in multiple sclerosis: effects on motor and cognitive functions. *Front Aging Neurosci.*

- National Institutes of Health, National Institute of Environmental Health Sciences. Autoimmune Diseases. Accessed May 1, 2021.
- Nieman DC, Sakaguchi CA.(2022) Physical activity lowers the risk for acute respiratory infections: Time for recognition. J Sport Health Sci ;11:648–55
- Ploeger HE, Takken T, de Greef MHG, Timmons BW.(2009) The effects of acute and chronic exercise on inflammatory markers in children and adults with a chronic inflammatory disease: A systematic review. Exerc Immunol Rev ;15:6–41.
- Rendon A, Schäkel K.(2019) Psoriasis pathogenesis and treatment. Int J Mol Sci. 20:1475.
- Roman II, Constantin AM, Marina ME, Orasan RI(2016) The role of hormones in the pathogenesis of psoriasis vulgaris. Clujul Med. 89:11-18.
- Roman II, Constantin AM, Marina ME, Orasan RI(2016) The role of hormones in the pathogenesis of psoriasis vulgaris. Clujul Med. 89:11-18
- S Gautam; B Chawla; S Bisht; M Tolahunase; R Dada. (2018)Impact of mindfulness based stress reduction on sperm DNA damage. J Anat Soc India
- Sanai SA, Saini V, Benedict RH, Zivadinov R, Teter BE, Ramanathan M, et al.(2016) Aging and multiple sclerosis. *Mult Scler.* 22:717–25.
- Sanai SA, Saini V, Benedict RH, Zivadinov R, Teter BE, Ramanathan M, et al.(2016) Aging and multiple sclerosis. *Mult Scler.* 22:717–25.

- Schurz H, Salie M, Tromp G, Hoal E, Kinnear CJ, Möller M.(2019) The X chromosome and sexspecific effects in infectious disease susceptibility. Hum Genomics. 13:2.
- Sharif K, Watad A, Bragazzi NL, Lichtbroun M, Amital H, Shoenfeld Y.(2018) Physical activity and autoimmune diseases: get moving and manage the disease. Autoimmun Rev.17(1):53-72.
- Shukla, A., Yadav, V. K., Yadav, V. P., Mishra, M. K., Maurya, R., Mishra, R. K., & Dubey, R. S. (2024). *Autoimmune Diseases in Women and Treatment Options*. 247–266.
- SmithBouvier DL, Divekar AA, Sasidhar M, Du S, TiwariWoodruf SK, King JK, et al.(2008) A role for sex chromosome complement in the female bias in autoimmune disease. J Exp Med. ;205(5):1099–108. 9.
- Smith-Bouvier DL, Divekar AA, Sasidhar M, et al.(2008) A role for sex chromosome complement in the female bias in autoimmune disease. J Exp Med. 205:1099-1108. 10.1084/jem.20070850
- Talal N.(1992) Sjögren's syndrome: historical overview and clinical spectrum of disease. Rheum Dis Clin North Am. 18(3):507–15. 10.
- V Dhawan; M Kumar; D Deka; N Malhotra; V Dadhwal; N Singh; R.(2018) Dada. Meditation & yoga: Impact on oxidative DNA damage & dysregulated sperm transcripts in male partners of couples with recurrent pregnancy loss. Indian J Med Res 148, S134-S139
- Valenzuela PL, Carrera-Bastos P, Castillo-Garcıa A, Lieberman DE, Santos-Lozano A, Lucia A.(2023) Obesity and the risk of cardiometabolic diseases. Nat Rev Cardiol 20:475–94.

- Van Den Hoogen F, Khanna D, Fransen J, Johnson SR, Baron M, Tyndall A, et al. 2013 classifcation criteria for systemic sclerosis: an American College of Rheumatology/European League against Rheumatism col- laborative initiative. Arthritis Rheum. 65(11):2737-47
- Wallin MT, Culpepper WJ, Coffman P, Pulaski S, Maloni H, Mahan CM, et al.(2012) The Gulf War era multiple sclerosis cohort: age and incidence rates by race, sex and service. *Brain.* 135:1778–85.
- Wang, Y. (2022). The Effects of Autoimmune Disease on the Women in the United States. *Highlights in Science, Engineering and Technology*, *8*, 210–214.
- Willard HF: (2003) Tales of the Y chromosome. Nature. 423:811-813. 1