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Rheumatoid Arthritis among Young Women: A Review of Diagnosis, Treatment, and Impacts

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ABSTRACT: Rheumatoid arthritis is a chronic autoimmune condition causing joint inflammation and damage, resulting in pain, swelling, and stiffness, often requiring a combination of medication, therapy, and lifestyle adjustments for management. Early diagnosis and intervention are crucial for reducing disability in rheumatoid arthritis (RA), hindered by limited access to specialists and evolving clinical features. Factors like acute phase reactants, serologic markers, and synovial tissue analysis aid RA diagnosis; treatment considerations in young RA patients involve methotrexate, hydroxychloroquine, sulfasalazine, and corticosteroids, with caution regarding conception, pregnancy, and lactation.Female hormonal factors can contribute to the disease's development.Female hormonal factors in disease development are complex, influenced by serum level fluctuations and interactions with environmental, immunological, genetic, and endocrine elements.Stress hormones like glucocorticoids and catecholamines modulate cytokine production, potentially affecting autoimmune disease activity and progression through systemic and local immune response modulation.Patients with rheumatoid arthritis can have higher risk of cardiovascular diseases due to systemic inflammation, compounded by factors like smoking and obesity.

Keywords: Rheumatoid Arthritis, Inflammation, Stress Hormones, Female Sex Hormones, Cardiovascular risks

I. INTRODUCTION:

This review looks closely at why rheumatoid arthritis (RA) affects women more often than men. It aims to thoroughly examine the specific aspects of the disease that relate to females and to understand the challenges doctors encounter when treating women with RA(Gerosa et al., 2008)**.**In younger adults, the male/female ratio of incident cases of RA is 1:5, but it becomes 1:1 after the age of 60 years, with women's incidence increasing steadily with age, while men's remains stable over the third through fifth decades and rises thereafter(1, n.d.).Rheumatoid arthritis, where the body produces autoantibodies like RF and ACPA, affects more women than men (3:1), though not as much as conditions like lupus(Taneja et al., n.d.).When we feel stressed, our body reacts through systems like the HPA axis and the sympathetic nervous system, releasing hormones like cortisol and adrenaline. These hormones, influenced by immune signals, can affect inflammation levels and may contribute to how autoimmune diseases start and progress(Elenkov & Chrousos, 2002).People with rheumatoid arthritis (RA) are more likely to develop cardiovascular diseases (CVD) compared to the general population. This higher risk of CVD is thought to be linked to the widespread inflammation often observed in RA patients(Rohrich et al., 2021).Scientists have explored whether using hormone treatments such as birth control pills or estrogen replacement therapy might influence the chances of developing rheumatoid arthritis (RA). However, the results regarding whether birth control pills could offer protection against RA have been mixed. Likewise, studies examining the risk of RA in women using estrogen replacement therapy after menopause have produced unclear results(11, n.d.)Choosing a diet rich in fruits and veggies while cutting out animal products could help protect against autoimmune conditions, while diets heavy on meat and light on fibres might raise the risk(Alwarith et al., 2019).

Pathogenesis of Rheumatoid Arthritis: Rheumatoid arthritis (RA) is a complex condition where joint inflammation happens due to a mix of genetics and environmental factors like smoking. It starts with the immune system mistakenly attacking the joints, causing inflammation and damage over time. This leads to joint pain, stiffness, and swelling. Cells and molecules in the joints contribute to this inflammation and can eventually lead to bone and cartilage damage(Taneja et al., n.d.).In rheumatoid arthritis (RA), immune cells

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like lymphocytes, neutrophils, and macrophages act as troublemakers, causing inflammation and damage in joints. They release substances called cytokines, which kickstart inflammation and break down cartilage, forming something called pannus. This pannus, fueled by extra blood vessels, lets more immune cells swarm into joints, making inflammation worse and wearing down bones. Meanwhile, other cells in the joints trigger more immune activity, leading to the production of substances that mark RA, helping doctors diagnose and predict the course of the disease(Alwarith et al., 2019b).

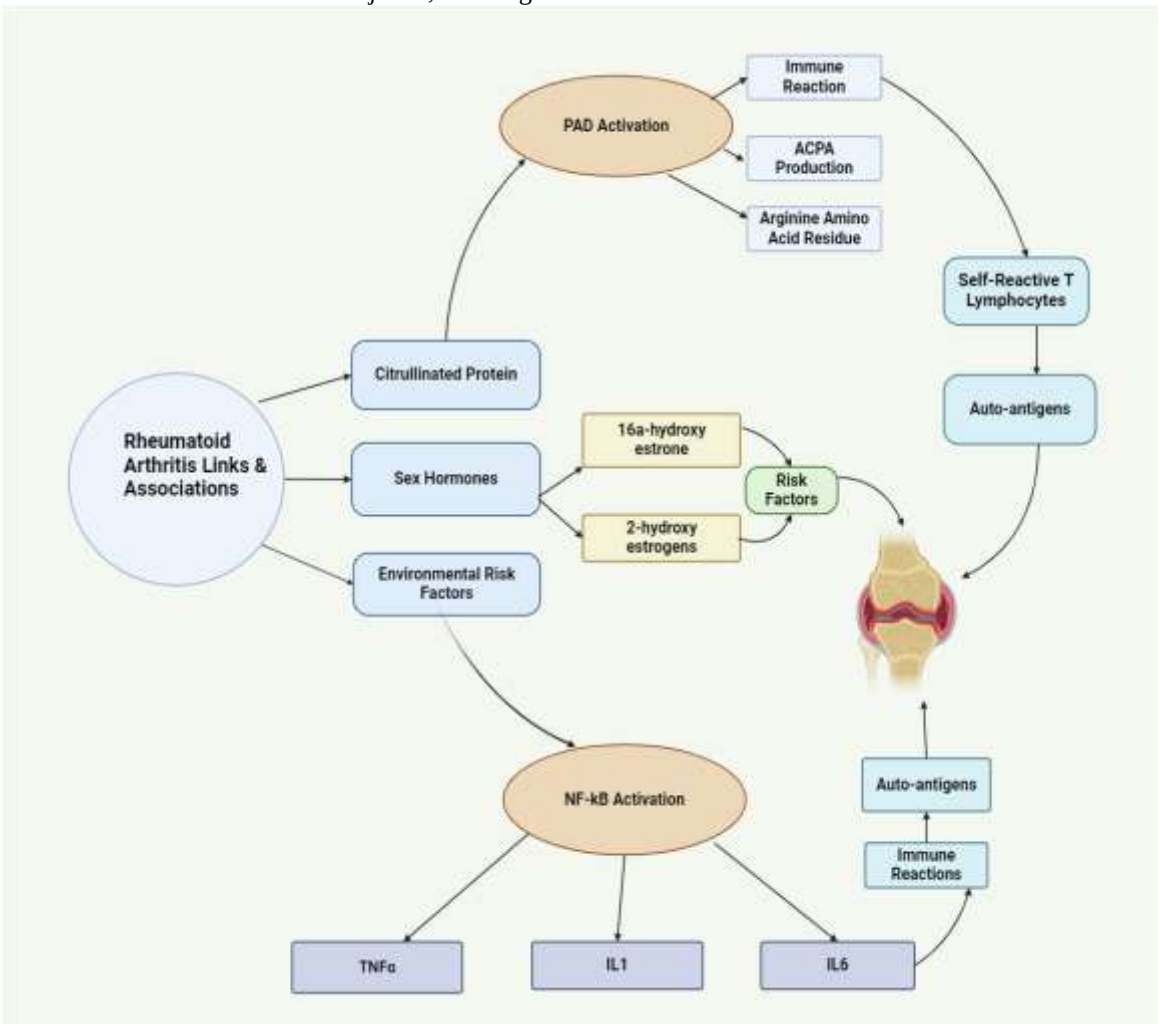

Figure No.1: Pathogenesis of Rheumatoid Arthritis

The Relationship Between Sex Hormones, the Immune System, and Autoimmune Diseases:

Studies show that while animal research suggests estrogen's involvement in autoimmune diseases through castration and hormone treatment, the real story is more complicated. Estrogen therapy doesn't consistently make autoimmune conditions like lupus worse, and some actually improve during pregnancy. Sex hormones affect the immune system, with estrogen boosting some responses while androgens and progesterone act as natural suppressors. Estrogen receptors on immune cells trigger signals that affect how cells grow and change, possibly affecting how autoimmune diseases develop and how severe they are. Also, estrogen can boost antibody production, while testosterone can't, showing how sex hormones and the immune system interact in complex ways(Gerosa et al., 2008).Interest in sex hormones (as estrogen) in RA has been revived over time since they were recently found to bias the immune response by protecting the survival of forbidden autoreactive clones and genes from sexual chromosomes. This phenomenon aligns with the

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high incidence of RA observed in female than male(Abda et al., 2016).Recent reviews looking at why RA might get better during pregnancy found something interesting: no studies have actually looked at how the extra estrogen or progesterone during pregnancy might affect RA. It's like we're missing a puzzle piece in understanding how hormones impact RA during pregnancy(Taneja et al., n.d.).Imagine estrogen, progesterone, and androgens as little messengers in our bodies. They have special keys that fit into specific locks on our cells. Once they unlock these receptors, it's like flipping a switch inside the cell, triggering a whole process that ultimately affects how certain genes act(Taneja et al., n.d.).The complexity of hormones like estrogen in rheumatoid arthritis reveals a complex interplay within the body's systems. Studies hint at estrogen's potential role in shaping the course of this autoimmune disease, offering insights into its pathogenesis. Beyond its traditional role in reproductive health, estrogen emerges as a key player in the realm of autoimmune disorders, shedding light on new avenues for research and treatment. This multifaceted hormone, once solely associated with gender, unveils its intricate connections to immunity and disease(Pradeep Kiran, 2019)

Impact of Estrogen, Progesterone, Oral Contraceptives & Stress Hormone:

In both men and women, our body's own hormones, androgens, act as moderators for the immune system, putting a check on certain responses. But when someone deals with rheumatoid arthritis (RA), it's like these hormone levels take a dip, possibly messing with how the disease ramps up and moves along(Alpízar-Rodríguez et al., 2017).Estrogen, a hormone found in individuals of both male and female sexes, has the capability to impact the physiological system through diminishing the quantity of distinct immune cells in the thymus and bone marrow. Furthermore, it exerts control over the generation of other critical immune cells. Additionally, it possesses the potential to trigger apoptosis in specific white blood cells.(Gerosa et al., 2008).Estrogen at normal levels helps B cells switch their immunoglobulin types, potentially worsening autoimmune diseases where the body makes harmful antibodies(Taneja et al., n.d.).Click or tap here to enter text. Elevated estrogen levels, particularly certain forms, are observed in RA patients. Studies have explored estrogen's effects on RA, with associations found with estrogen-related genes. Imbalances in estrogen metabolites may contribute to synovial cell proliferation in RA. Additionally, variations in androgen receptors in male RA patients hint at estrogen's involvement. Experiments blocking estrogen's cellular effects worsened arthritis in mice, indicating estrogen's independent role in RA beyond its function as a sex hormone(Pradeep Kiran, 2019).Progesterone can be in shaping our body's immune response.Progesterone acts like a superhero calming down inflammation in our bodies, potentially helping treat diseases like multiple sclerosis and rheumatoid arthritis. During pregnancy, it's like a guardian angel ensuring a healthy balance for both mom and baby(Taneja et al., n.d.)Progesterone, particularly in oral contraceptives, may offer protective effects against rheumatoid arthritis, with higher doses showing increased protection, while estrogen replacement therapy lacks similar benefits. The fact that medical records might not capture all the details emphasizes how important it is for researchers to delve deeper into understanding how estrogen, progestins, and rheumatoid arthritis are interconnected(11, n.d.) Stress hormones are like traffic controllers in your body. They can either calm down inflammation or rev up your immune system. Things like stress, exercise, and pregnancy can change how these hormones work, which affects autoimmune diseases. Understanding this helps doctors treat these conditions better (Elenkov & Chrousos, 2002).

Diagnosis:RA diagnosis delays may stem from patient hesitancy and healthcare limitations. Early RA differentiation from undifferentiated arthritis might benefit from elevated acute phase serum amyloid A (A-SAA) levels. Autoimmunity triggers immune attacks on normal tissues, causing chronic inflammation and functional impairments. (Gerosa et al., 2008)In RA, IgM RF and anti-CCP antibodies show similar prognostic significance in joint damage prediction. Immunohistology studies indicate synovial tissue macrophages and MMP-1 expression as early indicators of joint damage. Imaging studies reveal early cartilage and bone degradation, emphasizing the diagnostic value of IgM RF and anti-CCP antibodies in early RA detection. Immunohistologic analysis demonstrates potential for distinguishing RA from other arthritis based on cellular markers in synovial tissue(8, n.d.).

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Cardiovascular Risk Factor in Rheumatoid Arthritis Patient:

A patients have an elevated risk of cardiovascular diseases (CVD) due to systemic inflammation and classical risk factors. Current CVD risk prediction algorithms, like SCORE, may underestimate risk in RA, especially in those initially deemed low or intermediate risk. Recent findings indicate that younger RA patients face the highest relative CVD risk, while older patients have similar risks compared to age-matched counterparts. Women with RA also exhibit greater CVD risk, potentially exacerbated by early menopause. Standard risk calculators, which typically rely on age and gender, may inadequately estimate CVD risk in RA patients, warranting further investigation into tailored risk assessment approaches.(Rohrich et al., 2021).Pregnancy, with its hormonal changes, appears to offer protection against both the onset and activity of rheumatoid arthritis (RA), although statistical significance varies across studies. (Alpízar-Rodríguez et al., 2017).In rheumatoid arthritis (RA), while pregnancy planning isn't as critical as in other autoimmune diseases like SLE due to fewer complications, managing treatment during pregnancy and breastfeeding is crucial. Some drugs like azathioprine and cyclosporine are safe during pregnancy but not breastfeeding, while methotrexate, mycophenolate, and leflunomide are contraindicated. Anti-TNF-α and anti-B lymphocyte agents commonly used in RA treatment require careful timing and monitoring during pregnancy due to potentially fatal risks and lack of conclusive studies on breastfeeding safety(Gerosa et al., 2008). During pregnancy, autoimmune diseases like RA and MS often improve, but may worsen postpartum. The risk of new onset RA decreases by 70% during pregnancy but increases afterward, especially in the first three months. In MS, relapses decline during pregnancy, rise postpartum, and then return to pre-pregnancy rates. During pregnancy, the body tends to produce more of the soothing cytokines like IL-4 and IL-10, which can calm down the immune system and possibly ease autoimmune issues. Hormonal changes in late pregnancy, including increased cortisol and estrogen, may contribute to this improvement. However, postpartum hormonal shifts could trigger autoimmune flares by disrupting this balance, particularly in diseases like SLE.(Elenkov & Chrousos, 2002).Methotrexate, the mainstay for RA treatment, should be stopped before conception due to teratogenic risks. Biologics like TNF inhibitors are considered safer, but timing of withdrawal during pregnancy is crucial for minimizing risks to the foetus (Favalli et al., 2019).

Impact of Rheumatoid Arthritis on Pregnancy:

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Impact of Diet on The Management of Rheumatoid Arthritis:

The effects of a dietary regimen excluding meat, gluten, and lactose on individuals afflicted with long-standing rheumatoid arthritis (RA), juxtaposed against a well-balanced diet incorporating these constituents(Guagnano et al., 2021).Eating too much fatty food and processed meat can make certain inflammation markers in

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your body go up.Eating plenty of whole grains and fruits can help keep these markers low.(Alwarith et al., 2019a). Gluten- free diet like root vegetables, nuts & seeds, fruits etc. have positive impact on the management of rheumatoid arthritis. The Cretan Mediterranean Diet, abundant in olive oil, cereals, vegetables, fruits, and legumes, also improves RA indicators significantly. Diet high in fats may alter gut bacteria composition and promote inflammation. The fibre-rich, low-fat nature of vegan diets likely mediates pathways that reduce joint inflammation and pain, as indicated by decreased CRP levels and improved inflammatory scores, emphasizing the necessity for randomized studies to objectively assess inflammation biomarkers with plant-based dietary changes.(Alwarith et al., 2019a).

II. DISCUSSION:

Sex differences in RA onset show a female preponderance during reproductive years, with onset typically rare in men under 40. Smoking may influence earlier onset in RF-negative women, while RF presence correlates with earlier onset in men. Disease severity and remission rates vary between sexes, with men showing higher remission rates. Age, particularly menopausal status, appears to impact outcomes more significantly than age alone. Radiographic damage onset occurs early, with no significant difference between sexes after 2 years.A notable association between IgA RF and higher age at RA diagnosis, distinct from IgM RF's association with younger age.These findings emphasize the need to consider individual autoantibodies, age, and sex in future RA studies. Such adjustments are crucial given potential variations in autoantibody prevalence across different ethnicities, especially with increasing migration trends.Changes in female hormones like menopause, early menopause, after childbirth, and using certain medications affect RA development by lowering estrogen levels suddenly. Controversies persist regarding systemic hormonal treatments like contraceptives and HRT, as well as other factors such as parity and breastfeeding. The timing of oestrogen exposure, alongside non-hormonal sex-related factors, may influence RA onset, warranting further research for precise preventive interventions in high-risk women. In early RA treatment, patients may receive sulfasalazine, HCQ, or MTX alone or combined, with some advocating low-dose corticosteroids to reduce joint damage. Newer therapies like leflunomide and cytokine-targeted treatments are emerging, with careful consideration needed for fertility, pregnancy, and lactation in younger patients. An inverse association between oral contraceptive (OC) exposure and RA development, with women experiencing a 44% risk reduction following OC use.Choosing plenty of fruits and veggies can ease RA symptoms by calming inflammation and boosting gut health. On the flip side, diets packed with animal products might aggravate RA because they tend to spark inflammation.

III. CONCLUSION:

To sum up, the differences we see between men and women in how rheumatoid arthritis (RA) starts and progresses highlight the importance of looking at each person's unique situation, including their age, gender, and specific antibodies. While women often experience RA more during their childbearing years, the changes that come with menopause and hormonal shifts play a big role too. Understanding how things like hormones, environment, and genes interact is key to finding ways to prevent RA, especially in women who are at higher risk. As we discover new treatments, we need to make sure they're safe for things like having babies or breastfeeding. And remember, eating plenty of fruits and veggies can help with RA, while foods like red meat can make it worse because they can cause inflammation. Right treatment therapy and balanced diet can manage the symptoms of rheumatoid arthritis.

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