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A scoping review of rheumatoid arthritis

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Abstract

The chronic inflammatory disease rheumatoid arthritis (RA), which mostly affects the joints, is linked to considerably lower lifestyle quality. For individuals Inhibitors of the Janus kinase (JAK), a recently formed family of oral tiny molecules medicines, are being used to treat RA patients who don't react to traditional therapy or biological treatment and provide an alternative. The prevalence of RA varies greatly; investigations in several European nations have revealed rates ranging from 0.5% to 1.0%; research has shown that the RA incidence in Europe and In North America, ranged from 0.5 to 1%. Many macrophages, tumor necrosis factor-alpha (TNF-alpha), interleukin (IL)-1, IL-6, and IL-17, among others, are cytokines, are crucial in the development of disease; In addition to being stimulated by cytokines, osteoclasts also break down bone. There are several well-known risk factors for negative results, including illness activity is high, early joint injury, and the presence of autoantibodies, and early diagnosis is crucial to the efficiency of the therapy process. Biologics like Inhibitors of TNF-alpha, IL-1, IL-6, CD20, and cytotoxic T-lymphocyte associated antigen (CTLA)-4 (abatacept), as well as infliximab (etanercept, adalimumab), anakinra (anakinra), and tocilizumab (tocilizumab) are also available have altered the course of disease over the past few decades.

Keywords: Janus kinase inhibitor, Rheumatoid arthritis, Iraqi patients, TNF-alpha inhibitors, CD20 inhibitors

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Introduction

As joint destruction is rarely visible in the early stages, an inflammatory disorder with a long history is rheumatoid arthritis (RA) with several etiologies, an autoimmune component, as well as the symmetrical involvement of several joints [1].

In the later stages of the disease, symptoms outside of the joints such as lung involvement, serositis, vasculitis, Felty's disease, peripheral neuropathy, and are frequently present with RA, a systemic disorder [2]. The widespread of RA varies greatly; investigations in several European nations have revealed rates ranging from 0.5% to 1.0%; research has shown that the prevalence of RA in Europe and the American continent was between 0.5 and 1% [3]. In the summer of 1975, a prevalence study of rheumatoid arthritis was conducted among people 16 and older in Iraqi regions that represented various ethnic and geographic groups. One percent of the 6999 people who were studied had definite rheumatoid arthritis [4].

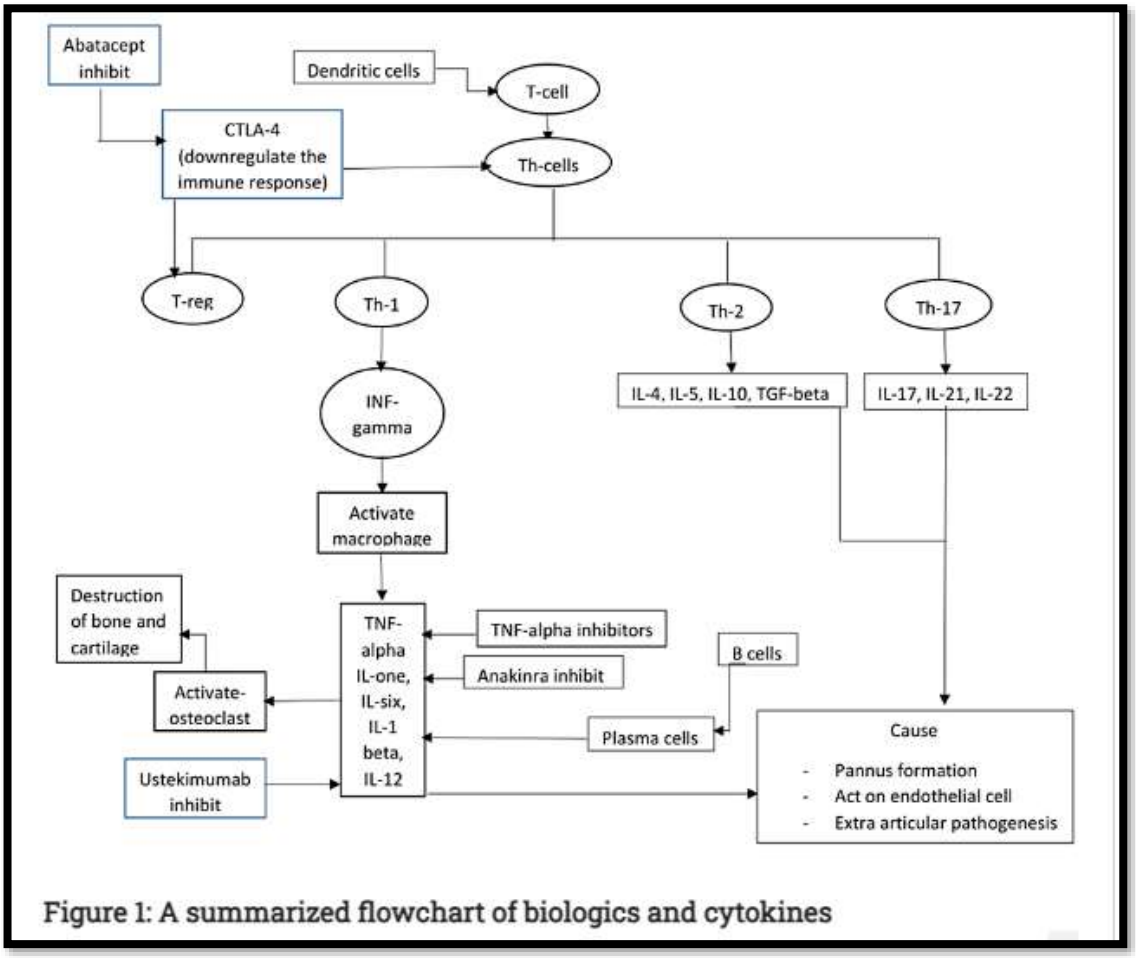

Figure 1: A summarized flowchart of biologics and cytokines

TNF, tumor necrosis factor, Th, helper T cells, transforming growth factor, interleukin, and regulatory T cells" (Cited by Patel et al., 2023) [5].

Rheumatoid arthritis in the province of Basra had clinical and serological characteristics that were comparable to those reported in various national and international investigations.
We noticed that there were more women than men (the ratio was 2:1) [5].
The various socioeconomic and developmental levels, genetic and environmental factors, as well as others, all contribute to this heterogeneity. Due to the lack of access to healthcare professionals, specialists, and/or medications in underdeveloped nations, people are recognized to have a bad prognosis and a severe clinical course when they have RA [6, 7]. Different targeted treatment modalities can be developed as a result of various manifestations and results. To the best of our knowledge, Al- Rawi et al, 1978 estimate of the prevalence of RA in Iraq is the most recent [8].
Although not directly life-threatening, it has a negative impact on the quality of life of patients and has serious economic ramifications for society [9], and as people get older, it occurs more frequently [10]. TNF-alpha, IL-1, IL-6, 1L-12, and CTLA-4 are examples of pro-inflammatory cytokines that damage the body's many organs. by causing joint degeneration, promoting pannus development, and inducing extra-rheumatic symptoms [11]. Figure 1 summarizes the biology of cytokines discussed above .

Pathophysiology of RA

Immunological processes, or the so-called pre-RA phase, have reportedly been known to take place years prior to the identification of joint inflammatory signs [12]. Modified self-antigens can develop from Biological and epigenetic interactions alterations on the chromosomal environmental and structural influences, as was the situation with vimentin, type 2 collagen, and immunoglobulin G (IgG). Peptidyl arginine deiminases could carry out citrullination, a post-translational modification, on these arginine-containing proteins [13,14]. Additionally, synovial infections or synovial hyperplasia can cause the release of cytokines, which can induce arthritic symptoms and altered self-antigens [15].
Histones, fibrin, fibronectin, Type II collagen, vimentin, and Epstein-Barr virus nuclear antigen 1 are examples of citrullinated proteins that the immune system no longer recognizes as self-structures because of the risk factors HLA-DR1 and HLA-DR4 [16]. Antigen-presenting cells (APCs), which are dendritic cells that have been prompted by starting an immunological reaction, take up antigens.
The entire complex moves where CD4+ helper T cells are activated in the lymph node. Additionally, B cells are present in the germinal core of the lymph node and are triggered by T cells sending back-and-forth signals; this immunological process is known as co-stimulation and includes interactions like those between CD28 and CD80/86 [17, 18].

By means of class-switch recombination or somatic hypermutation, B cells now begin to increase and transform into plasma cells that produce autoantibodies based on the receptors of the youngest cells [19]. The immune system produces autoantibodies, which are proteins that mistakenly target self-tissues and organs because the immune system can no longer distinguish between self and non-self-structures.

The Fc region of IgG, commonly known as the constant region, is the target of RF, one of the autoantibodies associated with RA that has been the subject of the most research. This IgM antibody has an 85% testing specificity in RA patients [20]. Along with complement protein and IgG, it also creates an immune complex that can move through a synovial fluid [21].

A study was carried out by Alsaber et al. (2020) to look into the relationships between RA activity and air pollution. However, it was found that nitrates and sulfur dioxide are significant dangerous elements for the onset of RA [22].

The pathogenesis of RA may be influenced by air pollution, according to a few molecular mechanisms. Free reactive oxygen species (ROS) could nuclear factor kappa B "NF-KB" activation, which causes T helper type 1 (Th1) to be activated and create the inflammatory cytokines Tumor necrosis factor-alpha (TNF), interleukin-1, and interleukin-1 and interleukin-6 (IL-1) [23]. These cytokines aid in the maturation of immature dendritic cells from latent monocytes, which in turn deliver self-reactive T lymphocyte auto-antigens, driving to migrate toward the target tissues, and promoting joint erosion and inflammation. Additionally, ROS promotes systemic inflammation and chronic lung disease and helps to citrullinate citrullinated peptides with arginine amino acid residues [24].

The skin produces 1,25-dihydroxy vitamin D3, which acts by stimulating the vitamin D receptor (VDR), as an immunomodulator, less frequently when ultraviolet B (UVB) exposure is reduced. Because of this, the immunomodulatory functions are subpar, which can lead to the onset of RA [25, 26]. The gut microbiota, The most densely populated bacterial population in the human body is another significant factor that has a significant impact on the pathogenesis of RA [27].

Additionally, intestinal dysbiosis, which sets off autoimmune pathways and mechanisms, is connected to the etiology of RA, including molecular imitation, changes in the permeability of the gut, through the activation of whether they are nod-like receptors (NLRs) or toll-like receptors (TLRs), stimulation of APC, encouragement mucosal inflammation is amplified, and T cell differentiation is inhibited [28].

Additionally, a large number of the complexity of the disease is aided by particular signaling molecules involved in inflammatory processes.

Tiny signaling proteins called Janus kinases (JAKs) have pathophysiological function significance since numerous therapeutic drugs can act as their molecular targets [29, 30]. In order to develop future medicines with excellent safety and efficacy profiles and to clarify all the pathogenic pathways, more study is therefore required.

Therapeutic Methods for RA

Over time, various treatment modalities have been employed to enhance patients' quality of life, lower risk, and assess the Efficacy and safety profile of novel active molecules. The ACR's "Treat to Target" guiding concept calls for selecting a successful treatment to bring about forgiveness or, alternatively, a decline in disease progression. Since it is impossible to reverse already-occurring erosions, the therapeutic intervention must be aggressive and quick [31].

In order to achieve an in addition to a very accurate diagnosis, the general approach to therapy includes prevention measures, non-pharmacological therapies, and pharmaceutical therapies. The pharmaceutical management of RA was updated by the 2021 ACR guideline for treatment, which offered seven compelling recommendations [32].

Role of Interleukins IL Inhibitors:

The IL inhibitor contributes to the blockage of IL receptors and models the development of the illness (33). The patients taking Anakinra demonstrated despite a 34% likelihood of treatment discontinuation linked to the drug, there was a 42% likelihood of an American College of Rheumatology (ACR20) response, including a substantial decline in ESR [34]. The inflammation-promoting cytokine IL-6 binds to receptors and sets off mechanisms for intracellular signaling that have an adverse effect on osteoclast activation, cytokine production, and joint inflammation as well as the progression of the disease [35].

Elevated atherosclerosis, infection, and pancytopenia risk have been associated with tocilizumab, a humanized monoclonal antibody that inhibits cytokine production aimed at IL-6 receptors in both their soluble and membrane versions [36]. Rash, headaches, and digestive issues were among the tocilizumab-related side effects, and it was discovered that the occurrence was higher in the control group than in the tocilizumab-treated patients [37].

Ethical Approval

Not required.

Conflicts of Interest

The authors declare that he has no competing interests.

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Study registration

Not required.

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