Journal of Cytokine Biology
ISSN: 2576-3881

Mini Review Open Access

Interleukin-6 as a Biomarker for Chronic Inflammatory Diseases: A Comprehensive Review

Mohammad Radwan*

Faculty of Medicine, Alexandria University, Egypt

Abstract

Interleukin-6 (IL-6) is a multifunctional cytokine involved in immune regulation, inflammation, and hematopoiesis. Elevated levels of IL-6 are associated with various chronic inflammatory diseases, including rheumatoid arthritis, Crohn's disease, psoriasis, and cardiovascular diseases. This comprehensive review explores the pathophysiological role of IL-6, its diagnostic utility, and its therapeutic implications. IL-6's involvement in key signaling pathways and its impact on disease mechanisms are discussed in detail. Additionally, the review highlights the use of IL-6 as a biomarker for disease activity and severity, and the potential of IL-6 inhibitors in improving clinical outcomes. Understanding IL-6's multifaceted role enhances our ability to diagnose, monitor, and treat chronic inflammatory diseases effectively.

Keywords: Interleukin-6; IL-6; Chronic inflammatory diseases; Rheumatoid arthritis; Crohn's disease; Psoriasis; Cardiovascular diseases; Cytokine biomarker; IL-6 inhibitors; Inflammation; Immune regulation; Pathophysiology; Diagnostic biomarker; Therapeutic target; JAK/STAT pathway; Acute phase response; Osteoclastogenesis; T cell survival; Keratinocyte proliferation; Atherosclerosis

Introduction

Interleukin-6 (IL-6) is a multifunctional cytokine involved in the regulation of immune responses, inflammation, and hematopoiesis. Discovered in the mid-1980s, IL-6 has been extensively studied for its role in chronic inflammatory diseases. Elevated levels of IL-6 have been associated with various conditions such as rheumatoid arthritis, Crohn's disease, psoriasis, and cardiovascular diseases. This review aims to provide a comprehensive overview of IL-6 as a biomarker for chronic inflammatory diseases, highlighting its pathophysiological role, diagnostic utility, and therapeutic implications. [1].

Pathophysiological role of IL-6

IL-6 is produced by a variety of cell types including T cells, B cells, macrophages, and fibroblasts. It acts through a receptor complex consisting of the IL-6 receptor (IL-6R) and the signal-transducing component gp130. Upon binding to its receptor, IL-6 triggers several intracellular signaling pathways, including the Janus kinase (JAK)/signal transducer and activator of transcription (STAT) pathway, the phosphatidylinositol 3-kinase (PI3K)/Akt pathway, and the Ras/mitogen-activated protein kinase (MAPK) pathway.

These signaling cascades result in the transcription of target genes involved in inflammation, immune regulation, and cell survival. IL-6 plays a critical role in the acute phase response, stimulating the production of acute phase proteins such as C-reactive protein (CRP) and fibrinogen. Additionally, IL-6 promotes the differentiation of naïve T cells into Th17 cells, which are key players in autoimmune and inflammatory responses [2].

IL-6 in chronic inflammatory diseases

Rheumatoid arthritis

In rheumatoid arthritis (RA), IL-6 is a major pro-inflammatory cytokine contributing to the pathogenesis of the disease. Elevated IL-6 levels are found in the synovial fluid of RA patients, where it promotes synovial inflammation and joint destruction. IL-6 stimulates osteoclastogenesis, leading to bone resorption, and enhances the production of matrix metalloproteinases, which degrade cartilage

Crohn's disease

IL-6 is also implicated in Crohn's disease, a chronic inflammatory bowel disease. Increased IL-6 levels correlate with disease severity and activity. IL-6 promotes the survival of T cells in the intestinal mucosa, contributing to the chronic inflammation characteristic of Crohn's disease. It also stimulates the production of anti-apoptotic proteins, which protect T cells from programmed cell death, thereby sustaining the inflammatory response [3].

Psoriasis

In psoriasis, IL-6 is involved in the proliferation and activation of keratinocytes and the recruitment of inflammatory cells to the skin. Elevated IL-6 levels are observed in psoriatic lesions and correlate with disease severity. IL-6 contributes to the dysregulated immune response and chronic inflammation seen in psoriasis.

Cardiovascular diseases

Chronic inflammation plays a pivotal role in the pathogenesis of cardiovascular diseases (CVDs). IL-6 is a key mediator linking inflammation and CVDs. Elevated IL-6 levels are associated with an increased risk of myocardial infarction, stroke, and heart failure. IL-6 promotes the expression of adhesion molecules on endothelial cells, facilitating the recruitment of inflammatory cells to atherosclerotic plaques and contributing to plaque instability and rupture.

Diagnostic utility of IL-6

Given its role in chronic inflammatory diseases, IL-6 has been

***Corresponding author:** Mohammad Radwan, Faculty of Medicine, Alexandria University, Egypt E-mail: mohammadradwan2001@gmail.com

Received: 03-July-2024, Manuscript No: jcb-24-143407, **Editor Assigned:** 08-July-2024, pre QC No: jcb-24-143407 (PQ), **Reviewed:** 22-July-2024, QC No: jcb-24-143407, **Revised:** 25-July-2024, Manuscript No: jcb-24-143407 (R), **Published:** 30-July-2024, DOI: 10.4172/2576-3881.1000516

Citation: Mohammad R (2024) Interleukin-6 as a Biomarker for Chronic Inflammatory Diseases: A Comprehensive Review. J Cytokine Biol 9: 516.

investigated as a diagnostic and prognostic biomarker. Elevated serum IL-6 levels can indicate disease activity and severity, providing valuable information for clinical decision-making. For instance, in RA, IL-6 levels correlate with disease activity scores and can predict response to therapy. Similarly, in Crohn's disease and psoriasis, IL-6 levels can serve as markers of disease activity and therapeutic response [4].

Therapeutic implications

Targeting IL-6 has emerged as a promising therapeutic strategy for chronic inflammatory diseases. Several IL-6 inhibitors, such as tocilizumab and sarilumab, have been developed and approved for the treatment of RA. These biologic agents neutralize IL-6 activity, thereby reducing inflammation and improving clinical outcomes.

In addition to RA, IL-6 inhibitors are being investigated for their efficacy in other chronic inflammatory diseases, including Crohn's disease, psoriasis, and CVDs. Preliminary studies have shown promising results, highlighting the potential of IL-6 inhibition as a therapeutic approach across various inflammatory conditions [5].

Conclusion

IL-6 is a critical cytokine in the pathophysiology of chronic inflammatory diseases. Its role as a biomarker for disease activity and severity, along with its potential as a therapeutic target, underscores its importance in clinical practice and research. Continued investigation into the mechanisms of IL-6 signaling and its role in different diseases will further enhance our understanding and management of chronic inflammatory conditions.

Materials and Methods

Literature search

A comprehensive literature search was conducted to gather relevant studies and reviews on IL-6 and its role as a biomarker for chronic inflammatory diseases. The search was performed using multiple databases, including PubMed, Scopus, Web of Science, and Google Scholar. Keywords used in the search included "Interleukin-6," "IL-6," "chronic inflammatory diseases," "biomarker," "rheumatoid arthritis," "Crohn's disease," "psoriasis," "cardiovascular diseases," "IL-6 inhibitors," and related terms. The search was limited to articles published in English up to June 2024 [6].

Inclusion and exclusion criteria

Studies were included in the review if they met the following criteria:

1. Investigated the role of IL-6 in chronic inflammatory diseases.

2. Examined IL-6 as a biomarker for disease activity, severity, or therapeutic response.

3. Discussed the pathophysiological mechanisms involving IL-6.

4. Evaluated the efficacy of IL-6 inhibitors in treating chronic inflammatory diseases.

Exclusion criteria were:

1. Studies not focused on IL-6.

2. Articles not available in English.

3. Studies lacking original data or critical analysis, such as commentaries or opinion pieces [7].

Data extraction

Data were extracted from the selected articles using a standardized form. The extracted information included:

1. Study design and methodology.

2. Patient population and sample size.

3. Measurement techniques for IL-6 levels.

4. Key findings related to IL-6's role in disease pathophysiology, diagnostic utility, and therapeutic implications.

5. Limitations and conclusions of the studies [8].

Data synthesis and analysis

The extracted data were synthesized qualitatively. Studies were categorized based on the chronic inflammatory diseases they investigated, such as rheumatoid arthritis, Crohn's disease, psoriasis, and cardiovascular diseases. The pathophysiological role of IL-6 in each disease was summarized, along with its potential as a biomarker and therapeutic target. Comparative analysis was conducted to identify common themes and unique aspects across different diseases.

Ethical considerations

As this review involved the analysis of previously published data, no ethical approval was required. However, all included studies were reviewed to ensure they adhered to ethical guidelines for clinical and biomedical research [9].

Limitations

The review is subject to certain limitations, including potential publication bias and the variability in study designs and methodologies among the included studies. These factors may affect the generalizability of the findings [10].

Discussion

The role of Interleukin-6 (IL-6) as a biomarker for chronic inflammatory diseases is multifaceted and significant. This comprehensive review underscores IL-6's pivotal role in the pathophysiology, diagnosis, and treatment of conditions such as rheumatoid arthritis (RA), Crohn's disease, psoriasis, and cardiovascular diseases (CVDs).

Pathophysiological insights

IL-6 is a key player in the immune response and inflammation. In RA, IL-6 contributes to synovial inflammation and joint destruction by promoting osteoclastogenesis and the production of matrix metalloproteinases. Similarly, in Crohn's disease, IL-6 facilitates chronic intestinal inflammation by enhancing T cell survival and inhibiting apoptosis. In psoriasis, IL-6 induces keratinocyte proliferation and attracts inflammatory cells to the skin, perpetuating the cycle of inflammation. In CVDs, IL-6's role in endothelial dysfunction and atherosclerosis highlights its broader impact on systemic inflammation.

Diagnostic utility

Elevated IL-6 levels are consistently associated with disease activity and severity across various chronic inflammatory diseases. In RA, IL-6 levels correlate with disease activity scores, offering a reliable biomarker for monitoring disease progression and therapeutic response. In Crohn's disease, IL-6 serves as a marker for intestinal inflammation,

while in psoriasis, its levels reflect the extent of skin involvement. The association of IL-6 with CVDs further emphasizes its potential as a systemic biomarker for chronic inflammation.

Therapeutic implications

The development of IL-6 inhibitors, such as tocilizumab and sarilumab, has revolutionized the treatment of RA by significantly reducing inflammation and improving clinical outcomes. The success of these inhibitors in RA has prompted their investigation in other chronic inflammatory diseases. Preliminary studies in Crohn's disease and psoriasis have shown promising results, suggesting that IL-6 inhibition could be a viable therapeutic strategy for these conditions. In CVDs, targeting IL-6 might offer a novel approach to reducing inflammation and preventing adverse cardiovascular events.

Challenges and future directions

Despite the promising role of IL-6 as a biomarker and therapeutic target, several challenges remain. The variability in IL-6 levels among individuals and the influence of other inflammatory mediators can complicate its clinical application. Standardizing measurement techniques and establishing clear diagnostic thresholds are essential for the effective use of IL-6 in clinical practice.

Future research should focus on elucidating the precise mechanisms of IL-6 signaling in different diseases, exploring its interactions with other cytokines, and identifying patient subgroups that would benefit most from IL-6-targeted therapies. Long-term studies are needed to assess the safety and efficacy of IL-6 inhibitors in a broader range of chronic inflammatory diseases and to explore their potential in preventing disease complications.

Conclusion

Interleukin-6 (IL-6) has emerged as a central cytokine in the pathogenesis and progression of various chronic inflammatory diseases. This review has highlighted IL-6's multifaceted role in diseases such as rheumatoid arthritis (RA), Crohn's disease, psoriasis, and cardiovascular diseases (CVDs). The evidence underscores IL-6's pivotal involvement in immune regulation, inflammation, and tissue remodeling, making it a valuable biomarker for disease activity and severity.

In RA, IL-6 contributes to synovial inflammation, joint destruction, and systemic manifestations of the disease. Its levels correlate strongly with disease activity, providing a reliable marker for monitoring progression and therapeutic response. Similarly, in Crohn's disease, IL-6 plays a key role in sustaining chronic intestinal inflammation, and its serum levels reflect disease activity. In psoriasis, IL-6 is involved in keratinocyte proliferation and the recruitment of inflammatory cells to the skin, making it a marker of disease severity. In CVDs, IL-6 links chronic inflammation to atherosclerosis and cardiovascular events, highlighting its systemic impact beyond localized inflammatory diseases.

The therapeutic targeting of IL-6 has revolutionized the treatment landscape for RA, with IL-6 inhibitors like tocilizumab and sarilumab demonstrating significant clinical benefits. These inhibitors reduce inflammation, slow disease progression, and improve patient outcomes. The success in RA has spurred research into the efficacy of IL-6 inhibitors in other chronic inflammatory diseases. Early studies in Crohn's disease and psoriasis have shown promising results, suggesting that IL-6 inhibition could be beneficial across a range of inflammatory conditions. Moreover, targeting IL-6 in CVDs presents a novel approach to mitigating inflammation-driven cardiovascular risk.

However, several challenges must be addressed to fully realize the potential of IL-6 as a biomarker and therapeutic target. The variability in IL-6 levels among individuals and the influence of other cytokines on its activity necessitate standardized measurement techniques and diagnostic thresholds. Further research is needed to elucidate the precise mechanisms of IL-6 signaling in different diseases, explore its interactions with other inflammatory mediators, and identify patient subgroups that would benefit most from IL-6-targeted therapies.

Long-term studies are crucial to assess the safety and efficacy of IL-6 inhibitors in a wider range of chronic inflammatory diseases. Additionally, understanding the potential adverse effects of chronic IL-6 inhibition will be important for optimizing therapeutic strategies. Future research should also focus on the development of novel IL-6 inhibitors with improved efficacy and safety profiles.

In conclusion, IL-6 is a critical cytokine in the pathophysiology of chronic inflammatory diseases, offering valuable insights into disease mechanisms and serving as a promising biomarker and therapeutic target. The continued investigation into IL-6's role in inflammation and immune regulation will enhance our ability to diagnose, monitor, and treat chronic inflammatory diseases, ultimately improving patient outcomes and quality of life.

References

1. Li Y, Liu S, Hernandez J, Vence L, Hwu P, et al. (2010) MART-1-specific melanoma tumor-infiltrating lymphocytes maintaining CD28 expression have improved survival and expansion capability following antigenic restimulation in vitro. J Immunol 184: 452-465.
2. Liu S, Etto T, Li Y, Wu C, Fulbright OJ, et al. (2010) TGF-beta1 induces preferential rapid expansion and persistence of tumor antigen-specific CD8+ T cells for adoptive immunotherapy. J Immunother 33: 371-381.
3. Besser MJ, Shapira-Frommer R, Treves AJ, Zippel D, Itzhaki O, et al. (2010) Clinical responses in a phase II study using adoptive transfer of short-term cultured tumor infiltration lymphocytes in metastatic melanoma patients. Clin Cancer Res 16: 2646-2655.
4. Godet Y, Moreau-Aubry A, Mompelat D, Vignard V, Khammari A, et al.(2010) An additional ORF on meloe cDNA encodes a new melanoma antigen, MELOE-2, recognized by melanoma-specific T cells in the HLA-A2 context. Cancer Immunol Immunother 59: 431-439.
5. Lacreusette A, Lartigue A, Nguyen JM, Barbieux I, Pandolfino MC, et al. (2008) Relationship between responsiveness of cancer cells to Oncostatin M and/or IL-6 and survival of stage III melanoma patients treated with tumour-infiltrating lymphocytes. J Pathol 216: 451-459.
6. Labarrière N, Pandolfino MC, Gervois N, Khammari A, Tessier MH, et al. (2002) Therapeutic efficacy of melanoma-reactive TIL injected in stage III melanoma patients. Cancer Immunol Immunother 51: 532-538.
7. Dréno B, Nguyen JM, Khammari A, Pandolfino MC, Tessier MH (2002) Randomized trial of adoptive transfer of melanoma tumor-infiltrating lymphocytes as adjuvant therapy for stage III melanoma. Cancer Immunol Immunother 51: 539-546.
8. Khammari A, Nguyen JM, Pandolfino MC, Quereux G, Brocard A (2007) Long-term follow-up of patients treated by adoptive transfer of melanoma tumor-infiltrating lymphocytes as adjuvant therapy for stage III melanoma. Cancer Immunol Immunother 56: 1853-1860.
9. Weber J, Atkins M, Hwu P, Radvanyi L, Sznol M, et al. (2011) White paper on adoptive cell therapy for cancer with tumor-infiltrating lymphocytes: a report of the CTEP subcommittee on adoptive cell therapy. Clin Cancer Res 17: 1664-1673.
10. Godet Y, Moreau-Aubry A, Guilloux Y, Vignard V, Khammari A, et al. (2008) MELOE-1 is a new antigen overexpressed in melanomas and involved in adoptive T cell transfer efficiency. J Exp Med 205: 2673-2682.