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HYPERTENSION AND INTERLEUKIN 1 BETA, A POSSIBLE BIOMARKER?

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Abstract

Hypertension, or high blood pressure (BP), a chronic, preventable, non-communicable disease regarded numerously as a noteworthy danger sign for cardiovascular diseases (CVD). Evidence have showcased the connecting link between chronic inflammation and hypertension implementing that during body's phase of chronicity, the immune system of our body triggers cells, such as monocytes, macrophages, neutrophils promoting the secretions of inflammatory cytokines may be interleukin 1 beta (IL-β) causing vascular permeability under the building up and release of Radical Oxygen Species (ROS) which promotes sustained chronic condition of the vascular endothelium. Therefore, we envisage that this review will strengthen the public understanding regarding the pathophysiological mechanisms and correlation of interleukin 1 beta in hypertension.

INTRODUCTION

According to the World Health Organization (WHO), Hypertension, quoted frequently as the "the silent killer" released it's first-ever report on the 19th of September 2023 is considered Hypertension to be a definite devastating impact, globally and developing countries like India, is on a race against this silent killer [1]. The 2017 American Heart Association and the 2018 European Society of Hypertension state that hypertension is categorized and diagnosed when a person's blood pressure is measured twice and the systolic or diastolic (measured on two different days) readings are both greater than or equal to 140 mmHg. [2] In the world, hypertension is the primary risk factor for death, contributing to 10.8 million deaths in 2019. [3]. Oceania, sub-Saharan Africa, East, South, and Southeast Asia have all seen increases in hypertension. [4].

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Prevalence of Hypertension

After accounting for the size of the regional population, the overall prevalence of hypertension (HTN) in India was estimated to be at 29.8%. [5], in which the highest prevalence seen in Sikkim, Punjab, Arunachal Pradesh, Kerala and NCT of Delhi and lowest in Daman & Diu and Dadra & Nagar Haveli [6]

Currently Hypertension has been trending.

The findings from Geldsetzer et al. regarding sex-wise differences in awareness, treatment, and control among hypertensive individuals are fascinating. It's interesting to note that women may outperform men in these aspects, potentially due to factors such as regular BP measurements during antenatal care visits for women and perhaps greater hesitancy among men to seek out healthcare services, leading to fewer opportunities for hypertension screening.[7]

The observational study conducted by Roy et al., highlighting the higher rate of hypertension prevalence in rural populations compared to urban populations, sheds light on the intricate dynamics influencing health trends. This finding suggests that factors associated with urbanization, such as changes in lifestyle, dietary habits, and environmental factors, could contribute significantly to the rising incidence of hypertension. [8]

The cohort study highlighting the adoption of semi-urban or urban lifestyles, particularly in areas near Delhi NCR, and its correlation with higher consumption of foods high in calories, fats, and salt highlights the rising frequency of high blood pressure worldwide, particularly in nations with low and medium incomes are also known as low- and middle-income countries (LMICs).

The significant relationship between ambient and household air pollution, particularly due to the use of kerosene or solid fuels for cooking, and its association with hypertension, cardiovascular diseases (CVDs), and mortality is a serious issue for public health, particularly in low- and middle-income nations (LMICs). [9]

Pathophysiology of Hypertension

Multifaceted hypertension condition has intricated pathophysiological mechanisms which involve the complex network of relationships between the several hormonal systems and the neurological system in the body which comprises the immune system, the renin-angiotensin-aldosterone system (RAAS), natriuretic peptides, the sympathetic nervous system (SNS), and the endothelium role. [10]. Due to the increasing stress factor among the population, studies have captured the recognition in the medical community that inflammation has a significant role in the development of hypertension and the subsequent harm to target organs. The association between inflammation, enhanced permeability of the blood vessels and the generation of strong mediators such as Reactive Oxygen Species (ROS) underscores the intricate and dynamic nature of the immune response. This interplay is crucial in both normal immune defense mechanisms and the

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pathogenesis of inflammatory diseases, including those impacting the cardiovascular system [11] Multiple studies have demonstrated intricate immunological reactions that play a role in the inflammatory mechanism of hypertension, with data suggesting elevated inflammatory mediators even in individuals who are not yet hypertensive. In hypertensive conditions, chronic inflammation can induce endothelial dysfunction, leading to increased vascular permeability, via the production of reactive oxygen species (ROS). Interleukin 1 beta (IL-1β) and other pro-inflammatory cytokines can cause thrombogenesis, fibrosis, and the production of reactive oxygen species (ROS) inside endothelial cells, all of which are harmful to cardiovascular health.[12]

Interleukin 1 Beta and its mechanism of action

Interleukin-1β (IL-1β) is a crucial cytokine and a potent pro-inflammatory cytokine mediator during an infection or an injury leading to an inflammatory process [13]

A mind capturing study done by Osamu Takeuchi and Shizuo Akira showed illustrated the interleukin 1 beta pattern recognition receptors during an inflammation through the production within cells of the innate immune system, such as monocytes and macrophages. Pathogen -associated molecular patterns (PAMPs) molecular motifs, recognized by pattern recognition receptors (PRRs) present on immune cells, Macrophages express various PRRs on their cell surfaces, such as Toll-like receptors (TLRs) and NOD-like receptors (NLRs). These receptors can recognize specific PAMPs. When a PRR on a macrophage binds to a PAMP, it triggers a signaling cascade within the cell. The engagement of PRRs by PAMPs activates intracellular signaling pathways in macrophages. These pathways regulate gene expression and cause transcription factors called nuclear factor-kappa B (NF-κB) to become activated. Genes expressing pro-IL-1β are among those whose transcription is aided by the active transcription factors. As a result, monocytes, which are macrophages, synthesize the inactive pro-IL-1β protein. The production of pro-IL-1β alone is not sufficient for the release of active IL-1β. Inflammasomes are activated to carry out additional processing. Multiprotein complexes known as inflammasomes cause caspase-1 to become active, cleaving pro-IL-1β into its active, mature version (IL-1β). After being processed, the macrophage releases active IL-1β, which then could promote inflammation. Strongly acting as an inflammatory mediator, IL-1β can affect several elements of the immune response, for example, an augmentation of immune cells at the site of injury or infection.[14]

Likely interferences of Interleukin 1 Beta in Hypertension

A prominent role for interleukin-1beta (IL-1β) in the etiology of different forms of hypertension is beginning to emerge. One pro-inflammatory cytokine that is essential to the body's immunological response is IL-1β. [15].

In hypertension, the phenotypic changes that vascular smooth muscle cells (VSMCs) experience aid in the advancement of the disease. The shift from a contractile to a synthetic phenotype, which is marked by enhanced migration, proliferation, and extracellular matrix formation, is one important alteration. This phenotypic switch is driven

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by various factors including mechanical stretch, oxidative stress, inflammatory cytokines, and growth factors [16].

In hypertension, the extra cellular matrix (ECM) remodeling occurs because of chronic inflammation and mechanical stress on the vessel wall. Interleukins, TNF-α, and ROS are examples of inflammatory mediators that can promote the production and release of extracellular matrix (ECM) proteins by fibroblasts, endothelial cells, and vascular smooth muscle cells (VSMCs). [17] Indeed, interleukins have attracted a lot of notice due to their involvement in inducing changes in vascular smooth muscle cells (VSMCs) and the extracellular matrix (ECM), particularly in the context of hypertension and vascular remodeling.[18]

Interferences of Interleukin 1 Beta in other chronic conditions

Elevated levels of IL-1β are associated with dyslipidemia, perhaps reinforcing low-grade inflammation. Furthermore, given its significant regulatory role, IL-1β may help anticipate the early beginning of cardiovascular disease. [19]

A study mentions that there is an association between IL-1β and the progression of atherosclerotic plaques probably because the expression of IL-1β becomes particularly high in complicated or advanced atherosclerotic plaques. [20]

The results of two experiments demonstrated that an engineered mouse with an IgG1 iso-class IL-1β antibody showed potent was created with IL-1 activity regulation in mind for in vivo application. The mouse demonstrated a significant limitation of cardiac enlargement and dysfunction following an experimental non - reperfused myocardial infarction, which must have been caused by the inflammasome's inhibited caspase 1. [21]

Studies have indicated that the only conditions for which IL-1 blockers are authorized are cryopyrin-associated periodic syndromes and rheumatoid arthritis. [22]

Studies related to acute and chronic inflammatory diseases such as as gout, type 2 diabetes, heart failure, recurrent pericarditis, rheumatoid arthritis, and smoldering myeloma where gain-of-function mutations in caspase-1 activity, have 1β neutralization appears to be effective in managing these diseases [23]

Polymorphism of IL-1Beta in Hypertension

After examining a field survey conducted in a few Chinese counties, Guo Huang and colleagues theorized that blood pressure and an IL-1β gene variant may be related. Their findings indicated a strong correlation, solely in males, between the IL-1β (−511) polymorphism and SBP, suggesting the involvement of the interleukin 1 family in the pathophysiology of hypertension. [24]

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A coronary angiography study carried out in Sheffield and London, Sheila E. Francis and colleagues examined the interleukin (IL)-1 cluster genes' allele frequencies and found that IL-1RN2 was strongly related with single vessel disease, which may have been a contributing cause to hypertension. [25]

M R Khawaja conducted an association analysis on 500 Pakistani Pathan participants, suggesting that the IL-1 β -511C/T and IL-1 RN 86 bp VNTR polymorphisms were not relevant in the genesis of hypertension. [26]

After doing research on IL-1B C-31T polymorphism in the Japanese population, Atsumi Yanagisawa and colleagues concluded that hypertension is linked to the TT genotype of the polymorphism.[27]

Nevertheless, a different study found no connection between hypertension and the IL-1B-31T polymorphism.[28]

Gorący J at al. had found a specific finding from a study done in the Polish population, suggesting that there was a proven correlation with hypertension, unfortunately no correlation between interleukin-1 gene cluster polymorphisms and coronary artery disease that was shown by angiographical means. [29]

CONCLUSION

In summary, the information highlights the IL-1β's function in the pathogenesis of hypertension, particularly through its involvement in ROS-mediated inflammatory signaling. IL-1β can initiate and perpetuate inflammatory responses within the vasculature, leading to endothelial dysfunction, vascular smooth muscle cell (VSMC) activation, and extracellular matrix (ECM) remodeling. The insights gained from various studies highlighting the function of IL-1β in hypertension offer promising avenues for the development of novel therapeutic strategies. Given the link between IL-1β and the immune pathways involved in chronic diseases, including hypertension, further exploration of IL-1β as a potential therapeutic target is warranted.

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