Elevated Th17 & IL 23 in Hypertensive Patients with Acutely Increased Blood Pressure

Thesis

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Ahmed ElNagar Ahmed Basry

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List of Abbreviations

Abb.	Full term
ACE	*Angiotensin-converting enzyme*
Ang II	*Angiotensinii*
AP-1	*Activating protein-1*
APC	*Antigen-presenting cells*
APCs	*Antigen presenting cells*
ASH	*American Society of Hypertension*
ATP	*Adenosine tri phosphate*
BAFF-R	*B cell-activating factor receptor*
BB	*Beta blocker*
BHS	*British Hypertension Society*
BP	*Blood pressure*
CBC	*Complete blood count*
CCB	*Calcium channel blocker*
CD45RO	*Memory cell marker*
CD69	*Activation marker*
CIAS1	*NLRP3*
COX-2	*Cyclooxygenase 2*
CpG odn	*CpG oligodeoxynucleotides are short single-stranded synthetic DNA*
CTL	*Cytotoxic T cell*
D	*Diuretic*
DAMPs	*Damage-associated molecular pattern molecules*
DASH	*Dietary Approaches to Stop Hypertension*
DBP	*Diastolic Blood pressure*
DC	*Dendritic cells*
DNA	*Deoxyribonucleic acid*
DOCA-salt	*Deoxy-corticosterone acetate-salt*
EC	*Endothelial cells*
ELISA	*Enzyme-linked immunosorbent assay*
ESC	*European Society of Cardiology*

List of Abbreviations cont...

Abb.	Full term
ESH	*European Society of Hypertension*
HAART	*Highly active antiretroviral therapy*
HDL	*High-density lipoprotein*
HGM	*Haemoglobin*
HIV	*Human immunodeficiency virus*
HMGB1	*High mobility group box 1 protein*
IFN	*Interferon gamma*
IgG	*Immunoglobulin G*
IL-17	*Interleukin 17*
IL23	*Interleukin 23*
iNOS	*Inducible nitric oxide synthase*
IRF	*Interferon regulatory factor*
ISH	*International Society of Hypertension*
JNC8	*Eighth Joint National Committee*
LDL	*Low-density lipoprotein*
L-NAME	*Nitro-L-arginine-methyl-ester*
MAPKs	*Mitogen-activated protein kinases*
MCP-1	*Monocyte chemo attractant protein-1*
MMF	*Mycophenolate mofetil*
MR	*Mineralo-corticoid receptors*
MyD88	*Myeloid differentiation*
NAD(P)H	*Nicotinamide adenine dinucleotide phosphate*
NF-κB	*Nuclear factor kappa-light-chain-enhancer of activated B cells*
NICE	*National Institute for Health and Care Excellence.*
NK-Tcell	*Natural Killer T*
NLR	*Leucine-rich repeat*
NLRP3	*Multiprotein oligomer*
PAMPs	*Pathogen-associated molecular patterns*

List of Abbreviations cont...

Abb.	Full term
PB	*Peripheral blood*
PEBP	*Phosphatidyl ethanolamine-binding protein*
PerCEP	*Peridinin chlorophyll*
PRR	*Pattern recognition receptors*
PVN	*Para ventricular nucleus*
rAAs	*Renin-angiotensin-aldosterone system*
RAG1	*Recombination-activating gene 1*
RIG-I	*Retinoic acid-inducible gene I*
SBP	*Systolic Blood pressure*
SGOT	*Serum glutamic-oxaloacetic transaminase*
SGPT	*Serum glutamic pyruvic transaminase*
SHR	*Spontaneously hypertensive rats*
SOD	*Superoxide dismutase*
STATA	*Software program*
T cell receptor	*TCR*
TC	*Total cholesterol*
TG	*Triglycerides*
Th17	*T helper cell 17*
TLR	*Toll-like receptors*
TNF	*Tumor necrosis factor-alpha*
TRIF	*TIR-domain-containing adapter-inducing interferon-β*
UK	*United Kingdom*
VSMC	*Vascular smooth muscle cells and*
WBC	*White blood cells*
WHO	*World Health Organization*

INTRODUCTION

As a chronic medical condition characterized by elevated blood pressure, hypertension is recognized as a major risk factor for a variety of life threatening diseases including stroke, myocardial infarction, heart failure and aortic aneurysm. And most of these severe complications occur in the hypertensive patients with a sudden increase of blood pressure ***(Guzik et al., 2007).***

In Egypt hypertension is with prevalence rate of 26.3% among the adult population. Its incidence increases with aging, around 50% of Egyptians over the age of 60 years have hypertension ***(Hasan et al., 2014).***

The pathophysiology of the sudden/acute increase of blood pressure in hypertensive patients is not clearly characterized. Despite enormous progress in hypertension research, the precise etiology of blood pressure elevation remains unknown in the vast majority of hypertensive patients.

While dysfunction in cardiovascular control centers including the kidney, the vasculature, and brain can coordinately contribute to sustained hypertension. The involvement of immune activation in hypertension has been well demonstrated by many research groups ***(Jiandong et al., 2015).***

Consistently, the activation of inflammatory cells is found in the peripheral blood of hypertensive patients ***(Dorffel et al., 1999).*** Inflammation and immune response, mediated by T lymphocyte can directly lead to vascular remodeling and increase of blood pressure. Macrophages and T cells infiltrate in the heart, the vasculature, and the kidney during hypertension ***(Wenzel et al., 2011).***

Enhanced expression of adhesion molecules on the blood vessels in these organs contributes to inflammatory cell accumulation by permitting increased leukocyte extravasation. In turn, these infiltrating mononuclear cells secrete or induce several pro-hypertensive cytokines including IL-6, IL-17, and TNF-α ***(Ates et al., 2014).*** Al adoptive transfer studies ***(Guzik et al., 2007)***

Th17 is a recently discovered subgroup of helper T cell characterized by the secretion of IL-17. It is believed that Th17 may play a role in the pathogenesis of hypertension. However, its underlying mechanism is still unknown ***(Schiffrin, 2010).***

In the recent study, demonstrated an increased level of Th17 in hypertensive patients with acute increases of blood pressure, which is probably caused by the increased plasma IL-23. The characterization of its pathophysiology might be beneficial for the prevention and therapy of the sudden/acute increase of blood pressure in hypertensive patients ***(Jiandong and Steven, 2015).***

Aim of the Work

The aim of this study is To evaluate the role of Th17 and IL23 in the immune pathogenesis of hypertension.

HYPERTENSION

A pragmatic definition of hypertension, is the level of blood pressure for which investigation and management do more good than harm ***(Neil, 2015).***

In 2010, high BP was the leading cause of death and disability-adjusted life years worldwide ***(Forouzanfar et al., 2017).***

In most national and international guidelines the threshold for the diagnosis of hypertension is a systolic blood pressure measured in a clinic or office of at least 140 mm Hg, a diastolic blood pressure of at least 90 mm Hg, or both ***(James et al., 2014).***

Blood Pressure is categorized into 4 levels on the basis of average BP measured in a healthcare setting: normal, elevated, and stage 1 or 2 hypertension (Table 1).

Table (1): Categories of BP in Adults

BP Category	SBP		DBP
Normal	and	<120 mm Hg	<80 mm Hg
Elevated	and	120–129 mm Hg	<80 mm Hg
Hypertension			
Stage 1	or	130–139 mm Hg	80–89 mm Hg
Stage 2	or	≥140 mm Hg	≥90 mm Hg

(Whelton et al., 2017)