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Estimation Relationship Between Interleukin-17 With Oxidant - Antioxidants Status Among Patients With Hypertension

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Abstract: Vasculitis characterized by immune cell infiltration is an important mechanism in the development of hypertension and cardiovascular disease.The role of IL-17 in hypertension is controversial So, This study aimed to observe and clarify the role of IL-17 in hypertension patients and its link with oxidative stress – antioxidants.The sample of this study consists of 30 patients (18 male ,12 female) and 30 apparently healthy individuals(18 male ,12 female) . The results showed an elevated mean sera level of IL-17 (966.04 pg/ml), in Patients with hypertension as compared with the control (213.37 pg/ml), with significant difference ($p \leq 0.05$) While show marked decrease in level of (NO and GSH) in Patients with hypertension as compared with the control ($p \leq 0.05$). It was found negative correlation between IL-17 , NO and GSH**.**

Keywords: Hypertension, IL-17, Nitric oxide, Glutathione

Introduction

Hypertension control is defined as achieving a blood pressure of less than 140/90 mmHg in individuals who are being treated for hypertension(Maimaris et al 2013). While uncontrolled hypertension was defined as an average SBP ≥140 mmHg or an average DBP ≥90 mmHg, among those with hypertension(Wyatt et al 2008). nThiQar Governorate, southern Iraq, a study conducted in 2012 on some primary health care centers in the city of Nasiriyah showed that 46.1% of the study population suffer from high blood pressure, and only 17.7% of them have controlled blood pressure. (Al-Lami et al 2012 ; Ali et al 2015). Hypertension is a major health problem, especially because the symptoms are not visible. Most people get hypertension without being aware of it. Modifier factors such as obesity, overweight

measured by body mass index, visceral adiposity measured by waist circumference, increased age, are now well known to be correlated with the high prevalence of hypertension (Dibby, 2015 ;Haneen and Khalid). Elevated formation of reactive oxygen species in the vascular wall is a major feature of cardiovascular disease and contributes to endothelial dysfunction and vasculitis .(Dominguez et al 2010; Higashi et al 2009).The corrilation between increased production of ROS and hypertension has been explained through enhanced inactivation of the vasodilator nitric oxide (NO) by superoxide radical (O2 -) (Grossman, 2008; Kopf et al 2008). Glutathione acts as a major thiol-disulfide redox buffer for the cell .Synthesis of GSH is catalyze through c-glutamyl cysteine syntheses (c-GCS) and GSH syntheses. c-GCS transcription and activity are regulated by many factors and processes such as GSH conjugation, GSH depletion , antioxidants, , inflammatory cytokines, oxidative stress , and nitrosative stress.(Wu et al 2004). Ulrich et al 2019 ,They focused on the cooperative roles of salt, IL-17, and the inflammatory response in autoimmune diseases and hypertension.

Materials and methods

This study has been conducted at AL-Hussein Teaching Hospital   in Thi-Qar , at the period between 16/1/2021 to 25/4/2021. It included (60) subjects, (30)   control(18 male ,12 female) and (30)   patients (18 male ,12 female) . A 3 mL-blood sample was pulled from each (patients and controls) IL-17 was determine by ELISA (Enzyme Linked Immunosorbent Assay) using ready kits manufactured by Elabscience company(USA).) NO was determine according to the method of (Dervisevic et al 2012). GSH was determine according to the method of(Ellman, 1959).

Statistical Analysis:

The statistical analysis was done using spss v 23 the results were expressed as mean ± standard deviation (mean ± SD). T test was used to compare parameters in studied groups Pearson's correlation was applied to determine the relationship among the present study parameters. P-values (P≤0.05) were consideredstatistically significant.

Result

In this work, it was specified the effect of this disease (hypertension) on the IL-17 ,NO and GSH. 6.7 % of patients have normal blood pressure (BP), 10% have high-normal blood pressure, 60% have grade 1 hypertension and 28% have grade 2 hypertension as shown in Table 1-1.

Table 1-1 Explain the classification of hypertensive patients based on office blood pressure (BP) measurement

Category	No. (%)	SBP (mmHg) Mean ±SD	DBP (mmHg) Mean ±SD
Normal BP	2(6.7%)	<130	<85
High-normal BP	3 (10%)	130–139	85–89
Grade 1 hypertension	18(60%)	140–159	90–99
Grade 2 hypertension	7(23.3%)	≥160	≥100

(Table 1-2) showed elevated level of IL-17in patients with hypertension as compared with the control with significant difference (p≤0.05) While show marked decrease in level of (NO and GSH) in Patients with hypertension as compared with the control (p≤0.05).

Table(1-2):- concentrations of IL-17,NO and GSH in (control) and(patients) groups

Parameters	Patient (n= 25) mean±SD	Control (n=25) mean±SD	p.value
IL-17 (pg/ml)	966.04±92.37	213.37± 32.46	0.000
NO(µmol/mL)	4.56±0.67	7.30±1.02	0.001
GSH(µmol/L)	402.50±93.09	540.76±82.21	0.000

Table (1-3) and figures (1-1), (1-2)Explain thecorrelation between IL-17 and other parameters in this studies .It was found negative correlation between IL-17 , NO and GSH).

Table (1-2) Correlation between IL-17 and other parameters this studies .

IL-17 with	R	Results

| NO	- 0. 72	negative correlation
GSH	- 0. 68	negative correlation
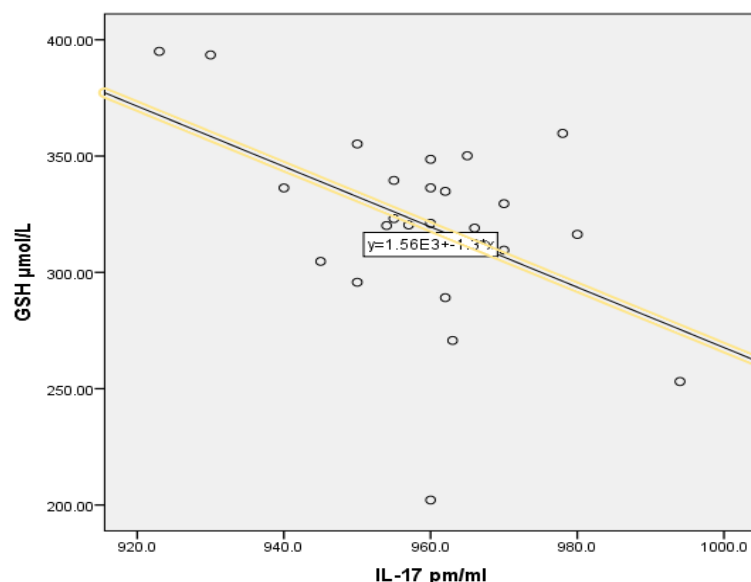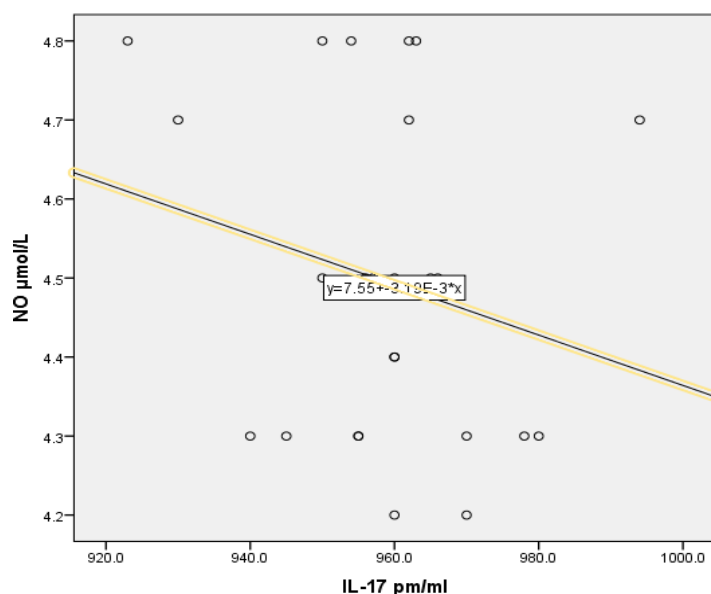
Figure (1- 1) shows the negative   correlation Figure (1- 2) shows the negative   correlation   between IL-17   and NO between IL-17   and GSH

Discussion

Interleukins, appear to play a role in peripheral organ damage in hypertensive individuals (as a major mediator of inflammation)(Daniela et al 2019). Actually, Vasculitis characterized by immune cell infiltration is an important mechanism in the development of hypertension and cardiovascular disease. (Eriksson et al ,2001).There are six known members of the IL-17 family. IL-17A is the most widely studied and has been implicated in the pathogenesis of multiple autoimmune and inflammatory diseases (Tesmeret al 2008). Recent evidence also supports a role for IL-17 in cardiovascular disease and hypertension (Eid et al 2009)Notably, the level of serum IL-17 in hypertensive patients was marked higher than in normal individuals (Madhur, et al 2010). Prehypertension is a transition stage from normotension to hypertension. A growing body of evidence indicates that chronic low-grade inflammation is a common pathological process and an important contributing factor to prehypertension (Virdis and Schiffrin 2003,Savoia and   Schiffrin,2007). However, few studies have investigated the relationship between prehypertension and the immune response.Weiet al2015 , were examined serum levels of IL-17 in prehypertensive patients and those with optimal BP. The serum level of IL-17 was significantly higher in the prehypertension group compared with the optimal BP group. Also the serum level of IL-17 in the prehypertension

group was very close to those reported in the hypertension group.It is known from preclinical models that an imbalance between the production and degradation of reactive oxygen species is involved in the mechanisms of hypertension. Because excessive ROS enhances cellular processes such as differentiation and apoptosis and controls vascular tension and endothelial function, it contributes to endothelial dysfunction. (M. S. Finkelet al 1992).Oxidative stress results from decreased levels of antioxidant   and increased generation of reactive oxygen species,Inflammation, in turn, leads to endothelial dysfunction and atherosclerosis through ROS, a product of cellular and soluble immune factors. (T. A. Angelovichetal ,2015, A. Agita and M. Taha 2017, W. R. Taylor 1999). Consequently, ROS stimulates proinfammatory cytokine secretion, and lessening availability of NO (Q.-Z. Liaet al 2005).Studies have shown that inhibiting ROS reduce blood pressure by improving endothelial function through rising NO production .(Daniela et al 2019).Oxidative stress is linked with GSH oxidation and depletion, which has been observed in hypertensive subjects when comparison with normotensive individuals(Rodrigo et al 2007, Bessa et al 2009 , Redon et al 2003).It has been shown that higher blood pressure is linked with disorders in glutathione metabolism. Mononuclear cells from hypertensive subjects display marked lower GSH and higher GSSG levels than from the control group(Chaves et al 2007).

Conclusion

In this study, the association between serum Il-17,NO and GSH levels and hypertension is studied. Serum IL-17 levels is a marker of inflammation is significantly raised in cases of hypertension. In conclusion, it was found a significant association between hypertension and serum IL-17. Also it was found the oxidative stress plays a significant role in the pathogenesis of hypertension.

References

A. Agita and M. Taha, "Infammation, immunity, and hypertension,"Te Indonesian Society of Internal Medicine, 2017: 49.

Al-Lami F, Mousa A. Prevalence of undetected, untreated, and uncontrolled hypertension among attendants of primary health care centers in Nasiriya city, Iraq. in Proceedings of the 61st Annual Epidemic Intelligence Service Conference (EIS '12), p. 99, Centers for Disease Control and Prevention, Atlanta, Ga, USA, April 2012

Ali A. Saadon Al-Ghuzi ,Jasim N. Al-Asadi and Olfatjabbar , Hypertension in Nassiryia City: Extent and determinants of its control , Thi-Qar Medical Journal (TQMJ):Vol (9) 2015(1-13).

Bessa, S. S., Ali, E. M., &Hamdy, S. M..The role of glutathione S-transferase M1 and T1 gene polymorphisms and oxidative stress-related parameters in Egyptian patients with essential hypertension.European Journal of Internal Medicine.2009 , 20, 625–630.

Chaves, F. J., Mansego, M. L., Blesa, S., Gonzalez-Albert, V., Jimenez, J., Tormos, M. C., et al.. Inadequate cytoplasmic antioxidant enzymes response contributes to the oxidative stress in human hypertension.American Journal of Hypertension. 2007 , 20, 62–69.

D. G. Harrison, P. J. Marvar, and J. M. Titze, "Vascular infammatory cells in hypertension," Frontiers in Physiology,2012, 3: 128.

Daniela Maria Tanase ,Evelina Maria Gosav , SmarandaRadu, et al. Arterial Hypertension and Interleukins: Potential Therapeutic Target or Future Diagnostic Marker? International Journal of Hypertension, 2019,2019 :17

Dervisevic A, Babic N, Huskic J, et al. Concentration of nitric oxide in saliva of patients with rheumatoid arthritis. Int J Collab Res Intern Med Public Health. 2012;4(7):1442–51.

Dibby, H. J.. Blood group relationship with hypertension : AL-Qadisiya Medical Journal. ,2015 ,11(20), 7–12.

Dominguez, L. J., Galioto, A., Pineo, A., Ferlisi, A., Ciaccio, M., Putignano, E., et al. . Age, homocysteine, and oxidative stress: Relation to hypertension and type 2 diabetes mellitus. Journal of the American College of Nutrition, 2010 ,29, 1–6.

Eriksson EE, Xie X, Werr J, et al. Importance of primary capture and Lselectindependent secondary capture in leukocyte accumulation in inflammation and atherosclerosis in vivo.JExp Med. 2001;194:205–218.

Eid RE, Rao DA, Zhou J, et al. Interleukin-17 and interferon-gamma are produced concomitantly by human coronary artery infiltrating T cells and act synergistically on vascular smooth muscle cells. Circulation. 2009;119:1424–1432.

Ellman, G. L. Tissue sulfhydryl groups.Archeves Biochemistry and biophysics, **1959** 82, 70-77. Grossman, E.Does increased oxidative stress cause hypertension? Diabetes Care, 2008, 31(Suppl 2), S185–S189.

Higashi, Y., Noma, K., Yoshizumi, M., &Kihara, Y. Endothelial function and oxidative stress in cardiovascular diseases. Circulation Journal, 2009, 73, 411–418.

HaneenKadhimZaid, Khalid G. Al-Fartosi , Assessment of Atrial Natriuretic Peptide (ANP) and Lipid Profile for Hypertension Patients in Thi-Qar province, Iraq, University of Thi-QarJournal of Science (UTsci), 8,2021

Kopf, P. G., Huwe, J. K., & Walker, M. K.. Hypertension, cardiac hypertrophy, and impaired vascular relaxation induced by 2,3,7,8-tetrachlorodibenzo-p-dioxin are associated with increased superoxide. Cardiovascular Toxicology2008 , 8, 181–193.

Maimaris W, Paty J, Perel P, Legido-Quigley H, Balabanova D, Nieuwlaat R, McKee M. The Influence of Health Systems on Hypertension Awareness, Treatment, and Control: A Systematic Literature Review. PLoS Med 2013;10(7):e1001490.

Madhur MS, Lob HE, McCann LA, et al. Interleukin 17 promotes angiotensin II-induced hypertension and vascular dysfunction. Hypertension. 2010;55:500–507

M. S. Finkel, C. V. Oddis, T. D. Jacob, S. C.Watkins, B. G. Hattler, and R. L. Simmons, "Negative inotropic efects of cytokines on the heart mediated by nitric oxide," Science1992, 257 :pp 387– 389.

Q.-Z. Lia, Q. Denga, J.-Q.Lia, and G.-H. Yi, "Valsartan reduces interleukin-1h secretion by peripheral blood mononuclear cells in patients with essential hypertension," ClinicaChimicaActa, 2005. 355, pp: 131–136,.

Redon, J., Oliva, M. R., Tormos, C., Giner, V., Chaves, J., Iradi, A., et al. Antioxidant activities and oxidative stress byproducts in human hypertension. Hypertension.2003 , 41, 1096–1101.

Rodrigo, R., Prat, H., Passalacqua, W., Araya, J., Guichard, C., &Bachler, J. P..Relationship between oxidative stress and essential hypertension. Hypertension Research, 2007 30, 1159–1167.

Savoia C, Schiffrin EL. Vascular inflammation in hypertension and diabetes: molecular mechanisms and therapeutic interventions. Clin Sci. 2007;112:375–384

Tesmer LA, Lundy SK, Sarkar S, et al. Th17 cells in human disease. Immunol Rev. 2008;223:87–113

T. A. Angelovich, A. C. Hearps, and A. Jaworowski, "Infammation-induced foam cell formation in chronic inflammatory disease," Immunology & Cell Biology, 2015, 93: pp: 683–693.

Ulrich O Wenzel1 ,Marlies Bode1 , Christian Kurts and HeimoEhmke , Salt, inflammation, IL-17 and hypertension , British Journal of Pharmacology (2019) 176 1853–1863

Virdis A, Schiffrin EL. Vascular inflammation: a role in vascular disease in hypertension? CurrOpinNephrolHypertens. 2003;12: 181–187.

Wei Yao, MD; Yuemin Sun, MD; Xuechun Wang, MD; KaijunNiu.Elevated Serum Level of Interleukin 17 in a Population With Prehypertension. Journal of Clinical Hypertension.2015; 17 :770-774

W. R. Taylor, "Hypertensive vascular disease and infammation: mechanical and humoral mechanisms," Current Hypertension Reports, 1999 1:pp. 96–101,

Wu, G., Fang, Y. Z., Yang, S., Lupton, J. R., & Turner, N. D..Glutathione metabolism and its implications for health. Journal of Nutrition, 2004, 134, 489–492.

Wyatt SB, Akylbekova EL, Wofford WR, Coady SA, Walker ER, Andrew ME, et al. Prevalence, Awareness, Treatment, and Control of Hypertension in the Jackson Heart Study. Hypertension 2008;51:650-656.

Wu, G., Fang, Y. Z., Yang, S., Lupton, J. R., & Turner, N. D. (2004). Glutathione metabolism and its implications for health. Journal of Nutrition, 134, 489–492.