COMMENT

A link between white blood cell count and blood pressure levels

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There is increasing recognition that alterations in hematologic indices may strongly be linked to hypertension [1–4]. Current studies have focused on the relationship between white blood cell (WBC) count and blood pressure levels. Friedman et al. [5] showed that, in an exploratory study of 1031 persons observed to progress from normotension to essential hypertension and 1031 matched subjects who remained normotensive, the initial WBC count might be related to the development hypertension. Gillum and Mussolino [6] analyzed the data from the National Health and Nutrition Examination Survey (NHANES) I Epidemiologic Follow-up Study (NHEFS), and reported a significant increase of about 50% in risk of hypertension over approximately 10 years' follow-up in white men aged 25–74 years with $WBC > 8600$ compared to men with $WBC < 6200$ cells/mm^3 after adjusting for cardiovascular risk factors. However, no positive association was seen in black men. Among white women in this study, the initial moderate association found in the age-adjusted model was no longer statistically significant after multivariate adjustment. Sun et al. [7] proposed that, in the Cardiometabolic Risk in Chinese (CRC) study, WBC count could independently predict hypertension in Chinese adults. Nakanishi et al. [8] followed up Japanese male office workers aged 23–49 years over 4 years, and demonstrated that WBC count might be an important risk factor for hypertension, which was pronounced in non-smokers. On the other hand, Shankar et al. [9] reported that elevated WBC count was associated with incident hypertension among women and men independent of smoking and most traditional risk factors in the white cohort. Orakzai et al. [10] showed that higher systolic blood pressure, even within the normotensive range, was also associated with elevated WBC count. Ishida et al. [11] examined the data from the Iki City Epidemiological Study of Atherosclerosis And Chronic Kidney Disease (ISSA-CKD) during an average follow-up of 4.5 years, and found a close association between the WBC count and further development of hypertension in the general Japanese population. In addition, this association was significant after adjustment for the effects of confounding factors, such as age, gender, current smoking habits, current alcohol intake, regular exercise habits, obesity, elevated blood pressure, diabetes, and dyslipidemia. Schillaci et al. [12] also showed that the WBC count had a direct association with smoking status, serum triglycerides, body-mass index, and 24 hour blood pressure levels, and further presented that cardiovascular event risk increased by 24% for each 2000 cells/mm^3 increase in WBC.

In this issue of Hypertension Research, Mansoori et al. [13] investigated the relationships between hematologic indices and hypertension in a cohort of Iranian adults. All participants were drawn from the Mashhad stroke and heart atherosclerotic disorder (MASHAD) study [14]. The association between hematologic factors and hypertension was assessed in 3070 subjects with hypertension and 6634 subjects without hypertension using logistic regression analysis and a decision tree (DT) algorithm. The authors demonstrated that, among analyzed variables, age and WBC were the most significant factors for hypertension incidents. Also, females were more likely to have hypertension compared with males. In addition, in the DT model, age, followed by WBC, gender and platelet distribution width (PDW), had the most significant impact on the hypertension risk. The authors concluded that elevated WBC and PDW might be the most associated factors with severity of hypertension in

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the Mashhad general population as well as female gender and older age.

Recently, there have been several studies regarding the relationship between WBC components and blood pressure. Tatsukawa et al. [15] examined the relationship between WBC components and blood pressure in a Japanese population during 40 years' follow up, and demonstrated a significant association between increased neutrophil count and hypertension incidence among women. Liu et al. [16] examined a total of 28,850 initially hypertensive-free subjects, and found that 1824 subjects developed hypertension during the 6 year follow-up period. In addition, it was shown that the elevated neutrophil/ lymphocyte ratio (NLR) levels correlated with an increased risk of hypertension. In the meta-analysis, there was a significant increase in NLR levels in the hypertensive group in comparison to the control group [17]. It was also demonstrated that the NLR was elevated in the non-dipper hypertensive patients compared with the dipper hypertensive patients [17, 18]. Furthermore, Wang et al. [19] presented that the NLR might be a predictor of all-cause mortality and cardiovascular events in patients undergoing angiography or cardiac revascularization. Balta et al. [20], also proposed that the NLR might have a close correlation with vascular disease and its associated risk factors.

On the other hand, Siedlinski et al. [21] investigated the relationship between WBC types and blood pressure in the UK Biobank population using observational and genetic analyses. They concluded that high blood lymphocyte count may play a causal role in the development of hypertension. It was also shown that blood lymphocyte count might influence albuminuria, which could explain, at least in part, the underlying mechanism for the association. Kresovich et al. [22] investigated how the immune system might be influenced by hypertension status. They showed that, among hypertension-free women at baseline of the cohort study, higher B cell and lower CD4+ helper T cell proportion were associated with subsequent increased hazard of hypertension incidence, indicating that expansion of B cell and exhaustion of CD4+ helper T cell proportions may precede hypertension development. In addition, they observed that, compared to normotensive women, women with hypertension had higher circulating proportions of neutrophils and lower proportions of CD4+ helper T cells, natural killers, and B cells, suggesting that there might be differences in circulating WBC composition in women before and after hypertension diagnosis.

The underlying mechanisms responsible for the association between increased WBC count and hypertension are still uncertain. The WBC count is a useful inflammatory biomarker. Recently, there has been much evidence showing that chronic inflammation might have a crucial role in the progression of cardiovascular diseases [23, 24].

One hypothesis is that increased WBC count might reflect chronic inflammation, which could lead to endothelial dysfunction [25]. Other possible mechanisms might be arteriosclerotic changes [26, 27], vasoconstriction [28], greater sympathetic tone [5] and chronic kidney disease development [19, 29]. On the contrary, Kishimoto et al. [30] reported that the WBC count was not associated with flow-mediated vasodilation (FMD) of the brachial artery (an index of endothelial function) or nitroglycerine-induced vasodilation (NID) (an index of vascular smooth muscle function). They speculated that WBC count and vascular function assessed by FMD and NID might reflect different aspects of atherosclerosis. Further studies are necessary to assess more thoroughly the relationship between WBC count and vascular reactivity and its contribution to the development of hypertension.

In summary, the study of Mansoori et al. [13] clearly demonstrated that high WBC count was associated with an increased risk of incident hypertension in a large cohort study of Iranian adults (MASHAD study). However, the precise mechanisms responsible for the relationship remain undefined. Also, there might be age, gender and racial differences in the association. A better knowledge of the cellular mechanisms underlying the link between WBC count and blood pressure levels could lead to a greater understanding of the pathophysiology of hypertension, and provide more effective strategies for the prevention of hypertension incidents.

Compliance with ethical standards

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