

The relationship between hypertension and COVID-19 vaccine in the long term and occupational evaluation

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ABSTRACT

Introduction: Many cardiovascular complications, especially myocarditis and pericarditis, have been observed with vaccination. One of these cardiovascular complications is hypertension with a rate of 1-5%. Hypertension emerged in the acute period after vaccination and tended to be persistent in patients with advanced age and comorbid diseases. In this study, we aimed to examine the relationship between hematological, biochemical markers and demographic characteristics between healthy individuals who have never been vaccinated or vaccinated and patients with new-onset hypertension.

Material and Method: Patients diagnosed with new-onset hypertension and healthy COVID-19 vaccinated, and non-COVID-19 vaccinated control patients of similar age and number were included in the study. The relationship between hematological, biochemical and demographic data between newly diagnosed hypertension patients and healthy COVID-19 vaccinated, and healthy non-vaccinated patients was examined.

Result: 56.3% of newly diagnosed hypertension patients were female, 46.9% were primary school graduates, 37.5% were housewives, 81.3% had stress in their lives. Hypertension patients were older ($p<0.01$), had lower hemoglobin levels ($p=0.05$) and higher LDL-C levels ($p<0.01$) than healthy unvaccinated patients.

Conclusion: Although it is seen that the cause of hypertension cannot be attributed solely to the vaccine, since the hypertensive group was older, had a higher body mass index, hyperglycemia and hyperlipidemia compared to the healthy group, and the number of patients in the study was small, but being a housewife is the most important occupational group and stress is an important trigger. The majority of vaccinees were primary school graduates. Anemia and LDL elevation were found in hypertensive and vaccinated patients. To the best of our knowledge, it is one of the first studies to examine LDL elevation in vaccinated patients and the relationship between long-term newly diagnosed hypertension and vaccination, although confounding factors cannot be excluded.

Key words: COVID-19, vaccine, hypertension, LD.

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INTRODUCTION

COVID-19 infection, a corona virus associated with SARS-CoV-2, which was first reported from China towards the end of 2019, was accepted as a pandemic by the World Health Organization (WHO) in March 2020 [1]. It affected 219 million people in the world and caused the death of 4.5 million people. Many vaccines such as inactive, mRNA, vector adeno virus have been produced to prevent it [2]. It is known that 68.5% of the world population has been vaccinated and 30% of them have received a reminder dose [3]. Many cardiovascular complications, especially myocarditis and pericarditis, have been observed with vaccination [2]. One of these cardiovascular complications is hypertension with a rate of 1-5% [4]. Hypertension emerged in acute periods after vaccination and tended to be permanent in patients with advanced age and comorbid diseases [5].

There are recent studies examining the relationship between vaccine and COVID-19. However, there is no study examining the relationship between long-term hypertension and vaccination. In this study, we aimed to vaccination history in patients with new-onset hypertension, to examine other occupational and environmental exposures that may cause hypertension, and to examine the relationship between hematological, biochemical markers and demographic characteristics between healthy individuals who have never been vaccinated or vaccinated and patients with new-onset hypertension.

MATERIAL METHOD

Patients between the ages of 18 and 50, who applied to the internal medicine outpatient clinic of Mersin City Training and Research Hospital between November 01, 2023 and April 01, 2024 and whose blood pressure was found to be higher than 140/90 mm Hg in repeated measurements in the evaluations made by the internal medicine specialist and who were diagnosed with hypertension and who did not have additional diseases such as kidney disease, renovascular disease, hyperthyroid-hyperparathyroid- cushing etc. that may cause secondary hypertension. endocrinologic disease, obstructive sleep apnea syndrome [6] and control patients who applied to the Occupational

and Occupational Diseases outpatient clinic on the same dates and who were evaluated by the Occupational and Occupational Diseases specialist with physical examination, hematologic, biochemical tests and imaging methods and no disease was detected were included in the study. Patients with hypertension for more than 6 months; patients with renal disease, renovascular disease, endocrinologic diseases such as hypertroid-hyperparathyroid-cushing's disease, obstructive sleep apnea syndrome, and [7] additional diseases that may cause hypertension secondary to hypertension will be excluded from the study. The relationship between hematologic, biochemical, demographic, occupational and vaccination status of newly diagnosed hypertension patients and healthy control patients will be examined.

Patient and healthy control groups; glucose, hematologic (hemoglobin [Hb], white blood cell [WBC], lymphocyte, neutrophil and biochemical parameters (creatinine, urea, aspartate transaminase [AST], alanine aminotransferase [ALT], triglyceride, high-density lipoproteins [HDL], low-density lipoprotein [LDL], fibrinogen, age, gender, height, weight, Body Mass Index [BMI], occupation, occupational risks (chemical, noise, pressure, cold, vibration), COVID-19 vaccination, how many doses, and which vaccines were obtained retrospectively by scanning the files.

The compatibility of the variables in the patient and control groups with normal distribution was examined using the Kolmogorov-Smirnov test. Mean \pm SD (standard deviation) was used to define numerical variables and categorical variables were defined as number and percentage. The relationship between demographic, hematologic, biochemical values, occupation, occupational risks, vaccination status and doses between newly diagnosed hypertensive patients and healthy control group; t-test and Mann-Whitney U test were used to compare numerical variables, and Chi-square or Fisher's exact chi-square tests were used for categorical variables. Univariable and multivariable logistic regression was used to assess relationship between hypertension patients and other independent variables healthy vaccinated and unvaccinated patients. The significance level will be taken as $p \leq 0.05$.

Ethical approval was obtained from the non-interventional clinical ethics committee of Mersin University with the decision of the board dated 03 April 2024 and numbered 2024/343. The study was conducted in accordance with the Helsinki Principles. The

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RESULTS

Among the newly diagnosed hypertensive patients, 56.3% were female, mean age was 46.7 ± 11.2 years, 84.4% had BMI >25 , and 46.9% were obese. 46.9% were primary school graduates, 59.4% were non-smokers. 37.5% were housewives, 81.3% had frequent stress in their lives, 40.6% were exposed to cold and noise. Of the hypertension patients, 30 (93.8%) had COVID-19 vaccine, 11 (36.7%) had both vaccines, 19 (63.3%) had only BioNTech vaccine. There was no comorbid disease in the healthy vaccinated and unvaccinated control groups. In the hypertension group, 8 (25%) patients had additional diseases, 2 (6.25%) had diabetes mellitus, 2 (6.25%) had kidney disease, 2 (6.25%) had hypothyroidism and 2 (6.25%) had asthma, and no additional diseases such as malignancy were found. Since the study was a retrospective study, information about whether the patients had COVID-19, and their antibodies could not be obtained. All those with comorbid diseases were vaccinated and had hypertension. Demographic characteristics of hypertension patients is given Table 1. 20 (32.3%) of the vaccinated patients participating in the study received both vaccines, 1 (1.6%) only Sinovac, 41 (66.1%) only BioNTech.

Newly diagnosed hypertensive patients were overweight ($p=0.03$), had lower education levels ($p=0.02$), and higher urea ($p=0.03$) and creatinine ($p=0.04$) values than healthy and vaccinated patients. Newly diagnosed hypertension patients were older ($p<0.01$), overweight ($p<0.01$), had lower education levels ($p<0.01$), lower hemoglobin ($p=0.05$), glucose ($p<0.01$) and LDL-C ($p<0.01$) levels than healthy unvaccinated subjects.

Relationship between hypertension patients and healthy unvaccinated and healthy vaccinated patients is given Table 2.

Table 1. Demographic characteristics of hypertension patients

Features	N(%)
Age (years) mean \pm SD	46.7 \pm 11.2
Gender	
Female	18(56.3)
Male	14(43.6)
BMI kg/m ² mean \pm SD	29.5 \pm 6.1
18.5<	1(3.1)
18.5-25	4 (12.5)
25>	27(84.4)
30>	15(46.9)
Smoking	
Yes	13(40.6)
No	19(59.4)
Time Package/ Year Median (Min-Max)	0 (0-60)
Education	
Illiterate	2(6.3)
Primary School	15(46.9)
Secondary School	4(12.5)
High School	3(9.4)
University	8(25)
Systolic Blood Pressure mmHg mean \pm SD	153 \pm 16
Diastolic Blood Pressure mmHg mean \pm SD	93 \pm 10
Comorbidity	8(25)
Diabetes Mellitus	2(6.25)
Kidney Disease	2(6.25)
Hypothyroidism	2(6.25)
Asthma	2(6.25)
Occupation	
Housewife	12(37.5)
Officer	6(18.8)
Blue-Collar Worker	7(21.9)
Others	7(21.9)
Exposure	
Chemical	7(21.9)
Noise	13(40.6)
Vibration	13(40.6)
Stress	26(81.3)
Sleeplessness	10(31.3)
Cold	1(3.1)
Vaccination	30(93.8)
Single Dose	2(6.3)
2 Dose	8(25.0)
2> Dose	20(62.5)

BMI Body Mass Index

Table 2. Relationship between hypertension patients and healthy unvaccinated and healthy vaccinated patients

	Hypertension n=32	Healthy Vaccinated n=32	P value	Healthy Unvaccinated n=32	P value
Features					
Age (years)	46.7±11.2	43.3±4.8	0.1	26.3±8.9	<0.01
Gender					
Female	18(56.3)	15(46.9)	0.5	10(31.2)	0.04
Male	14(43.8)	17(53.1)		22(68.8)	
BMI kg/m ²	29.6±6.1	26.6±3.8	0.03	24.5±5.5	<0.01
Education	2(6.3)	0(0)	0.02	0(0)	<0.01
Primary school	15(46.9)	10(31.3)		2(6.3)	
Secondary school	4(12.5)	2(6.3)		9(28.1)	
High school	3(9.4)	14(43.8)		13(40.6)	
University	8(25.0)	6(18.8)		8(25.0)	
Vaccination	30(93.8)	32(100)		0(0)	
Total dose median (min-max)	3(0-5)	3(1-5)	0.6	0(0-0)	<0.01
Sinovace dose median (min-max)	1(0-2)	1(0-3)	0.7	0(0-0)	<0.01
BioNTech dose median (min-max)	2(0-4)	2(0-4)	0.8	0(0-0)	<0.01
Hemoglobin g/dl mean±SD	13.9±1.9	14.1±1.5	0.5	14.8±1.9	0.05
Hematocrit % mean±SD	41.6±4.3	41.6±5.4	0.9	43.8±4.8	0.06
WBC x10 ³ / uL mean±SD	8.0±2.2	8.0±2.0	0.9	7.5±1.7	0.3
Neutrophil x10 ³ / uL mean±SD	4.6±1.7	4.9±1.9	0.6	4.5±1.4	0.8

BMI: Body Mass Index, HDL-C: High-Density Lipoprotein-Cholesterol, LDL-C: Low-Density Lipoprotein-Cholesterol

Table 3. The age- and gender-adjusted univariable and multivariable logistic regression analysis between hypertension patients and healthy unvaccinated patients.

Features	Univariable		Multivariable	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	0.8(0.7-0.9)	<0.01	0.8(0.7-0.9)	0.02
Gender	0.3(0.05-1.3)	0.1	0.2(0.02-2.9)	0.3
BMI	1.0(0.9-1.1)	0.9	0.9(0.8-1.2)	0.8
Hemoglobin	0.9(0.6-1.4)	0.9	0.9(0.4-1.7)	0.6
LDL-C	0.9(0.9-1)	0.04	1(0.9-1)	0.04

BMI: Body Mass Index, LDL-C: Low-Density Lipoprotein-Cholesterol

In the adjusted multivariable logistic regression analysis, older age (OR: 0.8, 95% CI: 0.7-0.9, p: 0.002), and higher LDL-C (OR: 1, 95% CI: 0.9-1, p: 0.004) were statistically significant in hypertension patients compared with healthy unvaccinated patients. The age- and gender-adjusted univariable and multivariable logistic regression analysis between hypertension patients and healthy unvaccinated patients is given Table 3.

DISCUSSION

The Centers for Disease Control and Prevention (CDC) reported that hypertension is more common in men with a rate of 50% worldwide [8], and the World Health Organization (WHO) emphasized that advanced age and obesity are risk factors for hypertension [9]. In studies conducted in our country, it was found that hypertension was more

common in women with a rate of 36.1% [10]. After the age of 40 years, there is an increase in susceptibility to atherosclerosis and the possibility of developing hypertension due to the decrease in vascular elasticity and the gradual decrease in estrogen with age, especially after the age of 45 years in women [11]. In our study, the rate was higher in women with a rate of 56.3%, the mean age was 46 years and 84.4% were overweight, which was similar to studies conducted in our country.

In our study, hypertension was found to be significantly higher in vaccinated patients than in healthy controls. However, since the hypertensive group was older, had a higher body mass index, hyperglycemia, and hyperlipidemia than the healthy group, the cause of hypertension cannot be attributed to the vaccine alone.

In studies conducted in developing countries, the rate of hypertension was found to be high in housewives, and it was emphasized that this was due to the fact that housewives have a stressful life due to taking care of the household, having a lot of work to do during the day and putting their own health and wishes in the second plan [11, 12]. Stress causes the development of hypertension over time by causing vasoconstrictor hormone release and even recurrent elevations in blood pressure [13], and work stress is also considered among the causes [14]. In addition, studies have shown that one of the most important risk factors for blood pressure is smoking and genetic burdens [15, 16] and in our study, 40.6% of hypertension patients were smokers. Although many factors such as smoking, genetic burden, and comorbid diseases cannot be excluded, housewifery was the most common occupational group, and stress was the most important risk factor.

In many studies including Turkey, a negative relationship was found between education and vaccination hesitancy [17-19]. However, in a large-scale study conducted in 15 different cities in Turkey using state data, no correlation was found between education level and vaccination, but a positive correlation was found between university and primary school graduates and a negative correlation was found between illiteracy and secondary school graduation [20]. In our study, 46.9% of those with hypertension who were vaccinated were primary school graduates and

40.6% of healthy unvaccinated individuals were high school graduates.

Many studies in the literature have shown that there is a positive correlation between high blood pressure and hemoglobin concentration [21,22]. In a study conducted on 4,203,887 people in Korea at the 3rd month after vaccination, the rate of nutritional anemia was found to be higher in those who were vaccinated and especially higher in those who received mRNA vaccination [23]. In our study, anemia was found in hypertension-vaccinated patients compared to unvaccinated healthy patients, and 63.3% of the vaccinated patients received biotech vaccine. Our study shows that although hemoglobin elevation was expected due to hypertension in patients, anemia was found in hypertensive and vaccinated patients, similar to the study conducted in Korea.

In a study conducted in Iran on lipid panel after vaccination, no effect of vaccination on lipid panel was found [24], and in a study conducted in Japan, elevated triglyceride levels were found [25]. In our study, LDL level was not found to be significant between hypertension-vaccinated patients and vaccinated-healthy control patients, whereas it was found to be significant in the unvaccinated-healthy control group; although confounding factors such as dietary behaviors and physical activity cannot be excluded, we found that vaccination has an elevating effect on LDL cholesterol. We think that these may be due to the disruption of the balance between LDL catabolism and production due to various reasons, such as proprotein convertase subtilisin or kexin type 9 (PCSK9), which has an important effect on hepatic receptor-mediated LDL catabolism, and angiopoietin-like protein 3 (ANGPTL3) [26], which regulates LDL production from its precursor very low-density lipoprotein.

The limitations of the study include the fact that it was a retrospective, single-center study; therefore, the number of patients was small and confounding factors such as dietary habits and physical activity, comorbid diseases, genetic factors, smoking could not be excluded.

Although it is seen that the cause of hypertension cannot be attributed solely to the vaccine, since the hypertensive group was older, had a higher body mass index, hyperglycemia and hyperlipidemia compared to the healthy group, and the number

of patients in the study was small, but housewifery was the most important occupational group and stress was an important trigger. The majority of those who received vaccination were primary school graduates. Anemia and elevated LDL levels were found in hypertensive and vaccinated patients. Although confounding factors cannot be excluded to the best of our knowledge, is one of the first studies to examine LDL elevation in vaccinated patients and the relationship between long-term newly diagnosed hypertension and vaccination.

Author contribution

Study conception and design: SME, TO; data collection: SME, TO; analysis and interpretation of results: SME; draft manuscript preparation: SME. All

authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The study was approved by the non-interventional clinical ethics committee of Mersin University (Protocol no. 343/2024).

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Conflict of interest

The authors declare that there is no conflict of interest.

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