




The Effect of the Vaccination Status of RT-PCR+ Covid-19 Cases on Albumin, N/L Ratio, CRP, and D-Dimer Levels

RT-PCR+ Covid-19 Vakalarının Aşılama Durumunun Albümin, N/L Oranı, CRP ve D-Dimer Düzeylerine Etkisi

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ÖZET

Amaç: SARS-CoV-2, tüm dünyayı etkileyen yüksek ölüm oranlarına sahip bir pandemiyi nedenidir. Bu çalışmada Biontech ve Sinovac aşısı olmasına rağmen tekrar RT-PCR+ Covid-19 tanısı alan hastalarda N/L Oranları, CRP ve D-dimer düzeyleri araştırıldı.

Materyal ve Yöntemler: Geriye dönük çalışma, 43 Biontech ve 71 Sinovac aşısı olup tekrar RT-PCR+ Covid-19 tanısı alan toplam 114 hasta (n=114) ve sağlıklı kontrol grubu (n=60) ile gerçekleştirildi. Biontech veya Sinovac aşısı olan ve RT-PCR Testi (Real-Time Polymerized Chain Reaction) pozitif çıkan vakalar çalışmaya alındı. Hastaların rutin biyokimya, seroloji ve hormon test sonuçları Kontrol Grubu ile karşılaştırıldı. Veriler bilgisayarda SPSS22 programı ile analiz edilmiştir.

Bulgular: CRP, N/L ve D-dimer düzeyleri aşı yapılan 2 grupta kontrol grubuna göre istatistiksel olarak anlamlı düzeyde yüksek bulunurken, Sinovac Grubunda daha yüksek değerler saptandı (p<0.001). Aşılı gruplarda kontrol grubuna göre albümin düzeyleri daha düşük bulundu (p<0,001). Aşılı gruplarda prokalsitonin, AST, LDH ve lipaz düzeyleri Kontrol Grubuna göre anlamlı olarak yüksek bulunurken, lenfosit düzeyleri aşılı gruplarda daha düşüktü (p<0.001).

Sonuç: Sinovac aşısı grubunda N/L oranları, CRP ve D-dimer düzeyleri Kontrol Grubuna göre daha yüksek olmasına rağmen, Biontech ve Sinovac aşısı olmasına rağmen tekrar RT-PCR+ Covid-19 tanısı alan hastalarda albumin düzeyleri daha düşüktü.

Anahtar Kelimeler: Covid-19; biyoteknoloji; Sinovac; N/L, CRP, D-dimer

ABSTRACT

Aim: SARS-CoV-2 is the cause of a pandemic with high mortality rates affecting the entire world. In the present study, N/L Ratios, CRP, and D-dimer levels were investigated in patients who were diagnosed with RT-PCR+ Covid-19 again despite receiving the Biontech and Sinovac vaccines.

Materials and Methods: The retrospective study was conducted with a total of 114 patients (n=114) and a healthy control group (n=60) who had 43 Biontech and 71 Sinovac vaccines but were diagnosed with RT-PCR+ Covid-19 again. Subjects who were vaccinated with Biontech or Sinovac and whose RT-PCR Test (Real-Time Polymerized Chain Reaction) was positive were included in the study. The routine biochemistry, serology, and hormone test results of the patients were compared with those of the Control Group. The data were analyzed on the computer with the SPSS22 program.

Results: CRP, N/L, and D-dimer levels were higher in the 2 vaccinated groups at statistically significant levels when compared to the control group, but higher values were detected in the Sinovac Group (p<0.001). Albumin levels were found to be lower in the vaccinated groups when compared to the Control Group (p<0.001). Procalcitonin, AST, LDH, and lipase levels were significantly higher in the vaccinated groups when compared to the Control Group, while lymphocyte levels were lower in the vaccinated groups (p<0.001).

Conclusion: Although N/L ratios, CRP, and D-dimer levels were higher in the Sinovac vaccine group than in the Control Group, albumin levels were lower in patients who were diagnosed with RT-PCR+ Covid-19 again despite having Biontech and Sinovac vaccines.

Key words: Covid-19; Biontech; Sinovac; N/L, CRP, D-dimer

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INTRODUCTION

The SARS-CoV-2 Disease pandemic appeared in China/Wuhan at the end of 2019 (COVID-19). Many people have died since then (1). Because of its high contagiousness, people have had to be hospitalized and live in long-term quarantine. It still maintains its disease-causing effects by undergoing various mutations. Also, it was shown in many previous studies that Covid-19 and its variants cause high morbidity and mortality (2-4).

There are some publications on the changes that might occur in the blood values in case of relapse in cases where Biontech and Sinovac vaccines were administered during the Covid-19 pandemic, and regarding their importance. The pandemic forced scientists to find answers about vaccines and antiviral treatments to control the pandemic all over the world. Major global efforts were made to develop vaccines for the COVID-19 pandemic. For this reason, safe and effective prophylactic vaccines are urgently needed to stop the pandemic, which has had devastating medical, economic, and social consequences. Viral vector vaccines, nucleic acid-based (RNA&DNA) vaccines, German (Biontech-Pfizer), and inactive vaccines (Coronovac Sinovac) were actively used in Turkey during the COVID-19 pandemic (5).

The N/L ratios, CRP, and D-dimer levels were investigated in patients who were diagnosed with RT-PCR+ Covid-19 again despite receiving the Biontech and Sinovac vaccines.

MATERIAL AND METHOD

After the approval of Ankara city hospital(E1-21-2062), blood samples taken from 114 patients and 60 healthy volunteers who were diagnosed with Covid-19 again after receiving the Biontech or Sinovac vaccine were examined in the laboratory, and the data were analyzed.

The cases were divided into 3 groups as the healthy control group, and the Biontech and Sinovac Groups. Computed tomography results of the lungs of cases that were diagnosed with Covid-19 were examined. Those with positive RT-PCR (Real-Time Polymerized Chain Reaction) results were also included. Biochemical values, complete blood count parameters, White blood cell (WBC), neutrophile lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), LMR(lymphocyte monocyte ratio), CRP (c-reactive protein), D-dimer, and albumin values of all subjects that were included in the study were entered into a separate statistical program. Individuals who were under the age of 18, trauma patients, and pregnant women were excluded from the study.

The Statistical Package for Social Sciences for Windows, Version 22 (IBM, Armonk, NY, USA) was used for statistical analysis. The Kolmogorov-Smirnov Test was used for the normality of the variables. Non-normally distributed data were represented by the median (interquartile range) values.

The Mann-Whitney U-Test was used to compare the mean values between the two groups. Categorical variables were summarized as numbers and percentages in each category. The Chi-Square and Fisher's Exact Tests were used for categorical variables. Optimal threshold values of continuous age, CRP, NLR, PLR, and LMR were calculated by applying Receiver Operating Curve (ROC) analysis. The Binary Logistic Regression Analysis was used to determine the effect of age, gender, and all other important factors. Hosmer-Lemeshow Goodness-of-Fit statistics were used to evaluate the model fit and $p < 0.05$ was considered statistically significant.

RESULTS

The demographic data, chest tomography findings, and clinical findings are given in Table 1. Although the age, N/L Ratios, CRP, and D-dimer levels were higher in the Patient Group compared to the Control Group, albumin levels were found to be lower (Table 2).

When routine blood parameters were examined in Biontech and Sinovac Groups, WBC and neutrophil, NLR, CRP, D-dimer, Aspartat Aminotransferaz (AST), Gama glutamil transferaz (GGT), Troponin, and lipase levels were significantly higher in the Sinovac Group than in the Biontech Group, which received a total of 43 Biontech and 71 Sinovac

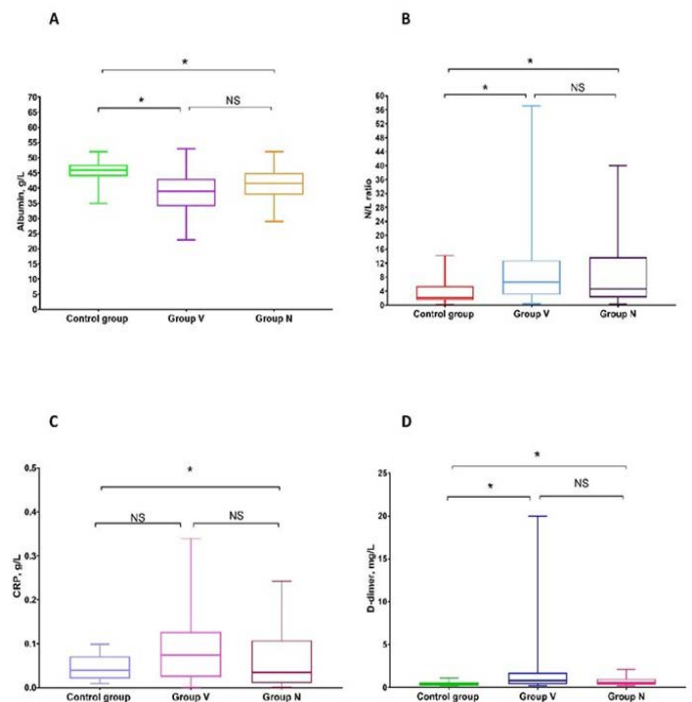


Figure 1. Comparison of Albumin (A), N/L ratio (B), CRP (C), D-dimer (D) levels of the control, Group V and Group N.

Table 1. Demographic results of Vaccinated with Biontech (Group B) and Vaccinated with Sinovac (Group S).

Characteristics	Total (n=114)	Group B (n=43)	Group S (n=71)	p Value*
Age, Median (IQR), range, years	65 (53-77), 26-95	56 (48-62), 28-95	68 (62-79), 26-95	0.977 ^a
Gender, male/female	34/26	29/14	29/42	0.007 ^b
PCR positive, (%)	101 (77.1)	37 (60.6)	64 (91.4)	0.505 ^a
Involment rate in CT				
<25%	87 (76.3)	37 (86)	50 (70.4)	0.057 ^a
25 – 50%	14 (12.3)	2 (4.7)	12 (16.9)	0.053 ^a
>50%	13 (11.4)	4 (9.3)	9 (12.7)	0.583 ^a
Time interval to become infected with COVID after vaccination				
0-3 month	54 (47.4)	25 (58.1)	29 (40.8)	0.073 ^a
3-6 month	35 (30.7)	9 (20.9)	26 (36.6)	0.078 ^a
6-9 month	25 (21.9)	9 (20.9)	16 (22.5)	0.841 ^a
Clinical course of the disease				
ICU	38 (33.3)	21 (48.8)	17 (23.9)	0.006 ^a
Hospitalized (non ICU)	47 (41.2)	7 (16.3)	40 (56.3)	<0.001 ^a
Discharged (taburcu)	29 (25.4)	15 (34.9)	14 (19.7)	0.072 ^a
Comorbidities				
Systemic hypertension, n, (%)	62 (54.4)	17 (39.5)	45 (63.4)	0.013 ^a
Diabetes mellitus, n, (%)	40 (35.1)	11 (25.6)	29 (40.8)	0.098 ^a
Congestive hearth disease, n, (%)	32 (28.1)	8 (18.6)	24 (33.8)	0.080 ^a
Chronic renal disease, n, (%)	9 (7.9)	3 (7.0)	6 (8.5)	0.777 ^a
Cancer, n, (%)	10 (8.8)	5 (11.6)	5 (7.0)	0.402 ^a
Chronic obstructive pulmonary disease, n, (%)	12 (10.5)	3 (7.0)	9 (12.7)	0.337 ^a
Signs and Symptoms				
Dyspnea	55 (48.2)	20 (46.5)	35 (49.3)	0.773 ^a
Dry cough	27 (23.7)	6 (14.0)	21 (29.6)	0.057 ^a
Diarrhea and vomiting	6 (5.3)	5 (11.6)	1 (1.4)	0.018 ^a
Joint pain	6 (5.3)	3 (7.0)	3 (4.2)	0.524 ^a
Weakness	25 (21.9)	5 (11.6)	20 (28.2)	0.039 ^a

aComparison of two groups based on Independent Sample T test, b Comparison of two groups based on chi square test. The significance level was set at $p < 0.05$. IQR: Inter Quantile Range, ICU: Intensive care unit

vaccines and were later diagnosed with Covid-19 again, but albumin and lymphocyte levels were found to be lower (figure1).

DISCUSSION

SARS-CoV-2 Disease, which started in China in 2019, has caused a challenging and threatening pandemic (COVID-19) worldwide with great health and economic losses. Many people have a history of a significant allergic reaction to a particular food, drug, or vaccine; for this reason, people are very concerned about these two approved vaccines all over the world (6). This article compares the blood changes of those who relapsed after receiving the Pfizer/Biontech and Sinovac vaccines.

Studies are reporting that two doses of Sinovac with different concentrations and different dosing schedules are tolerated well and moderately immunogenic in healthy adults aged 18-59 years (7). Most of the side effects of Sinovac were mild and the most common symptom was injection site pain. For the Sinovac vaccine to be fully effective, at least 2 doses of vaccine were recommended to be administered 1 month apart. Then, it was known that it was immunogenic and

protected from Covid-19.

Pfizer/Biontech vaccine was approved by the FDA and used in many countries. This vaccine is a priority in many countries. The side effects of the Pfizer/Biontech vaccine are natural reactions to foreign drug injection, including symptoms e.g. fever, muscle pain, and inflammation at the injection site, which are mediated by the innate immune system. When the neutrophils or macrophages of the body detect vaccine molecules, they release cytokines, which are chemical signals that trigger immune responses expressed as fever, chills, nausea, and muscle pain. No scientific data is showing that both vaccines provide full protection against the disease (8).

The mechanisms of coagulopathy in Covid-19 have not yet been elucidated fully. Inflammatory cytokines, lymphocyte cell death, hypoxia, and dysregulated immune responses induced by endothelial damage are considered to play roles in this respect. Bleeding tendency is rare even in cases with prolonged coagulation tests (9, 10). D-dimer levels were found to be associated with increased mortality. Post-vaccination D-dimer elevation was detected in some cases.

Table 2. Laboratory findings of patients group based on control group, Group B and Group S.

Characteristics	Control group (n=60)	Vaccinated with Biontech (Group B) (n=43)	Vaccinated with Sinovac (Group S) (n=71)	p Value*	p Value**
Age, Median (IQR), range, years	49 (42.8-60.8), 22-78	56 (48-62), 28-95	68 (62-79), 26-95	<0.001 ^a	C vs. GB, p= 0.275 C vs. GS, p< 0.001 GB vs. GS, p=0.001
Albumin, g/L	46 (44-48)	41 (34-44)	38 (34-42)	<0.001 ^a	C vs. GB, p< 0.001 C vs. GS, p< 0.001 GB vs. GS, p=0.982
Total protein, g/L	71 (68-73)	66 (60-70)	66 (61-70)	<0.001 ^a	C vs. GB, p< 0.001 C vs. GS, p< 0.001 GB vs. GS, p=1.000
Lymphocytes, x10 ⁹ /L	2.0 (1.5-2.7)	1.0 (0.4-1.8)	0.9 (0.5-1.4)	<0.001 ^a	C vs. GB, p< 0.001 C vs. GS, p< 0.001 GB vs. GS, p=1.000
N/L	2.1 (1.4-5.4)	5.6 (2.2-19.7)	7.3 (3.6-12.6)	<0.001 ^a	C vs. GB, p< 0.001 C vs. GS, p< 0.001 GB vs. GS, p=0.990
CRP, g/L	0.04 (0.02-0.07)	0.04 (0.01-0.12)	0.08 (0.03-0.14)	<0.001 ^a	C vs. GB, p=1.000 C vs. GS, p< 0.001 GB vs. GS, p=0.011
PCT, µg/L	0.03 (0.03-0.07)	0.06 (0.03-0.23)	0.11 (0.05-0.3)	<0.001 ^a	C vs. GB, p< 0.001 C vs. GS, p= 0.001 GB vs. GS, p=0.308
D-dimer, mg/L	0.36 (0.21-0.55)	0.59 (0.27-1.90)	0.99 (0.43-1.72)	<0.001 ^a	C vs. GB, p=0.001 C vs. GS, p< 0.001
GB vs. GS, p=0.392 Troponin I H ng/L	2 (2-3)	5 (2.5-43)	10 (3-38)	<0.001 ^a	C vs. GB, p< 0.001 C vs. GS, p< 0.001 GB vs. GS, p=0.537
Lipase, U/L	30 (25-37)	40 (28-73)	41 (30-68)	<0.001 ^a	C vs. GB, p= 0.005 C vs. GS, p< 0.001 GB vs. GS, p=1.000
AST, U/L	17.5 (14-23.8)	34 (26-52)	30 (21-52)	<0.001 ^a	C vs. GB, p< 0.001 C vs. GS, p< 0.001 GB vs. GS, p=1.000
GGT, U/L	20 (15-32)	40 (21-56)	34 (22-66)	<0.001 ^a	C vs. GB, p=0.012 C vs. GS, p< 0.001 GB vs. GS, p=1.000
LDH, U/L	201 (177-244)	298 (241-518)	332 (255-455)	<0.001 ^a	C vs. GB, p< 0.001 C vs. GS, p< 0.001 GB vs. GS, p=1.000
Lactate, mmol/L	1.5 (0.8-2.1)	2.0 (1.3-2.9)	1.7 (1.3-2.5)	0.005 ^a	C vs. GB, p=0.038 C vs. GS, p= 0.010 GB vs. GS, p=1.000

All values presented as Median (IQR). *Comparison of three groups, **Comparison of control, Vaccinated with Biontech (Group B) and Vaccinated with Sinovac (Group S) groups. aKruskal-Wallis analysis (analysis of variance) and bchi square test test. Non-parametric test for pairwise comparisons. The significance level was set at p < 0.05. C: control GB: group Biontech GS: group Sinovac

D-dimer was found to be higher in both vaccinated groups in the present study, but it was found to be significantly higher in the Sinovac Group than in the Biontech Group. This suggests that the Biontech Vaccine does not increase D-dimer levels more and protects it from possible thromboembolic events more than Sinovac.

Albumin is a protein synthesized by the liver and plays important roles in the nutrition and maintenance of plasma osmolarity (11). Juyi Li et al. reported that low albumin levels indicate the patient's poor nutritional status, which also reduces the immunity of the body, and the host's immune response to RNA virus infection is often weakened by

nutritional deficiencies, which might go undetected during clinical diagnosis and treatment (12). In patients with the diagnosis of Covid-19 and hypoalbuminemia, comorbid conditions might be the cause of low albumin levels (13). The low albumin levels in both vaccinated case groups might give an idea for the disease to be more severe. The fact that the albumin level was significantly lower in the Sinovac Group suggests that it is insufficient in preventing the disease.

CRP is among the inflammatory markers and is an acute phase protein synthesized by hepatocytes. Significantly elevated serum CRP levels in COVID-19 patients might be an indicator of excessive inflammatory stress and may contribute

to serious disease status (14). In the present study, it was found that CRP levels increased in COVID-19 patients in response to proinflammatory cytokines, which were also reported to be increased in a large part of previous studies. Greater increases were detected in the Sinovac group.

Elevated NLR is an increased risk factor for in-hospital mortality. In Covid-19 cases, while neutrophil increases, the decrease in lymphocytes results in increased NLR levels. There are publications associated with the severity of the disease with high NLR (15, 16). In the present study, increased NLR levels in both vaccine groups indicate the severity of the infection. In Biontech vaccine cases with Covid-19 detected again, the level of CRP increased less than those who received the Sinovac vaccine. This made us think that the Biontech vaccine has a positive effect on the inflammatory process.

CONCLUSION

Although the N/L ratios, CRP, and D-dimer levels were higher in the Sinovac vaccine group, the albumin levels were lower in patients who were diagnosed with RT-PCR+ Covid-19 again despite having Biontech and Sinovac vaccine.

LIMITATIONS

The present study had some limitations. Serial examinations could not be performed because of financial and logistical constraints on the patients. The sampling size was small and more extensive studies are needed in this regard.

Etik Kurul: Ethics committee approval was received for this study from the The local ethics committee of Konya Research and Training Hospital (Date: 2021/03/06, decision no: E1-21-2062).

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