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Letter to the Editor

Serum C reactive protein predicts humoral response after BNT162b2 booster administration

Although vaccination against coronavirus disease 2019 (COVID-19) is now considered the most efficient measure for preventing severe acute coronavirus disease 2 (SARS-CoV-2) infections and disease-related complications1, the humoral response to vaccines and its consequent efficacy may be strongly influenced by demographic and clinical variables2. Several recent studies have focused on specific clinical risk groups3,4, overlooking the impact that baseline inflammation may have on post-vaccine anti-SARS-CoV-2 antibodies response, that we have instead explored in this study.

Our study population consisted of 78 healthcare workers (median age, 45 years and interquartile range (IQR), 32–52 years;

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**Abreviations:** COVID-19, Coronavirus Disease 2019; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; IQR, Interquartile range.

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![Graph](https://doi.org/10.1016/j.jinf.2022.04.015)

Fig. 1. Correlation between the variation of serum anti-SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) spike trimeric RBD IgG antibodies and serum C reactive protein (CRP) in recipients of BNT162b2 vaccine booster.

SARS-CoV-2; severe acute respiratory syndrome coronavirus 2; RBD, receptor binding domain; CRP, C reactive protein.
54% females) recruited from the staff of Pederzoli Hospital in Peschiara del Garda (Italy), who received a booster dose (30 μg) of Pfizer/BioNTech BNT162b2 vaccine (Pfizer Inc., New York, US) 8 months after completing a homologous primary vaccination cycle with BNT162b2 (two 30 μg doses, 3 weeks apart). Venous blood was collected immediately before and 1 month after receiving the vaccine booster. The serum levels of anti-SARS-CoV-2 spike trimeric IgG were measured at both time points with Diasonic Trimeric spike IgG immunoassay on Liaison XL (DiaSorin, Saluggia, Italy); analytical sensitivity: 4.81 kBAU/L, whilst serum C reactive protein (CRP) was measured on pre-booster samples with a latex-enhanced immunoturbidimetric assay on Roche Cobas 6000 (Roche Diagnostics, Basel, Switzerland; analytical sensitivity: 0.3 mg/L, linearity: 0.6–350 mg/L). The variation of anti-SARS-CoV-2 spike trimeric IgG was expressed as ratio between pre- and post-booster serum antibodies levels. Results are shown as median and interquartile range (IQR), whilst the association between serum CRP and anti-SARS-CoV-2 spike trimeric IgG antibodies was tested with Spearman's correlation, using Analyse-it (Analyse-it Software Ltd, Leeds, UK). All subjects provided written informed consent for both receiving BNT162b2 vaccination and for participating in the serosurveillance study. This investigation was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Verona and Rovigo Provinces (59COVIDCESC; November 3, 2021).

The administration of BNT162b2 vaccine booster was effective to increase the serum levels of anti-SARS-CoV-2 spike trimeric IgG by nearly 40-fold (median increase, 38-fold; IQR, 20–78 folds), from 252 (IQR, 132–395) to 8555 (IQR, 4658–14,550) kBAU/L. A highly significant correlation was found between pre-booster serum CRP concentration and post-booster anti-SARS-COV-2 spike trimeric RBD IgG antibodies variation (r = 0.36; 95% CI, 0.15–0.54; p = 0.001), as shown in Fig. 1. In keeping with this finding, the median post-booster increase of anti-SARS-COV-2 spike trimeric RBD IgG antibodies was significantly higher in patients with serum CRP >3 mg/L (n = 7; increase: 54-fold; IQR, 26–92 folds) compared to those with serum CRP <3 mg/L (n = 71; increase: 37-fold; IQR, 19–78 folds; p = 0.025). Importantly, no significant association was found between serum pre-booster levels of CRP and anti-SARS-CoV-2 spike trimeric IgG (r = −0.20; 95% CI, −0.40 to 0.03; p = 0.082).

The results of this study show for the first time that the humoral response developing after receiving a BNT162b2 vaccine booster is significantly associated with pre-booster serum CRP levels. Notably, a similar association has been previously reported by Gianfagna et al. in people undergoing primary BNT162b2 vaccination1. Specifically, the authors found that subjects with higher CRP serum levels displayed a faster increase of anti-SARS-CoV-2 IgG levels after receiving two primary doses of BNT162b2. Combining these data with our novel findings it could hence be hypothesized that the extent of the humoral response after COVID-19 vaccination may be dependant (proportional) to baseline inflammation, as reflected by individual CRP levels.

In conclusion, the evidence emerged from this study (i.e., that measuring serum CRP may help predicting the BNT162b2 post-booster increase of anti-SARS-CoV-2 antibodies) could be used as valuable information for personalizing vaccine booster administration (both dosage and timing), thus enabling to optimize the worldwide use of COVID-19 vaccines.

**Author contributions**

All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

**Declaration of Competing Interests**

Authors state no conflict of interest.

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**References**

1. Mattuzzi C, Lippi G. COVID-19 vaccines efficacy in preventing or limiting SARS-CoV-2 infections. J Infect 2022 Jan 31;30163-4453(22)00051-2Doi: 10.1016/j.jinf.2022.01.033. Epub ahead of print.

2. Syed MA, AlQotba HA, Alnuami AS. Effectiveness of COVID-19 vaccines. J Infect 2022 Mar 25;163-4453(22)00121-9Epub ahead of print. doi:10.1016/j.jinf.2022.02.034.

3. Whitaker HJ, Tsang RS, Byford R, et al. Pfizer-BioNTech and Oxford AstraZeneca COVID-19 vaccine effectiveness and immune response among individuals in clinical risk groups. J Infect 2022 Jan 3;30163-4453(21)00664-2Epub ahead of print. doi:10.1016/j.jinf.2021.12.044.

4. Westrop SJ, Whitaker HJ, Powell AA, et al. Real-world data on immune responses following heterologous prime–boost COVID-19 vaccination schedule with Pfizer and AstraZeneca vaccines in England. J Infect 2022 Feb 4;30163-4453(22)00055-XEpub ahead of print. doi:10.1016/j.jinf.2022.01.038.

5. Gianfagna F, Veronesi G, Raj A, et al. Anti-SARS-CoV-2 antibody levels and kinetics of vaccine response: potential role for unresolved inflammation following recovery from SARS-CoV-2 infection. Sci Rep 2022;12:385.