Concentration of IgG against the Spike Receptor-Binding Domain predicts the viral neutralization activity of convalescent plasma and serum against SARS-CoV-2…

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Introduction

SARS-CoV-2 is the virus responsible for the Covid-19 pandemic, due to its rapid propagation and the initial lack of vaccines or appropriate treatments. Nowadays, despite different vaccines available, the main treatments are palliative, focused on supplemental oxygen and anti-inflammatory therapy.

Passive immunization could be an effective and economic treatment once standarized. It consists of the transfer of pathogen-specific antibodies to patients whose immune system has not originated a response yet. The donors' antibodies neutralize and attenuate pathogen replication. Besides, an antibody against the Receptor-Binding Domain of Spike (RBD) would block the interaction of the virus with ACE2 and its entry in the cell.
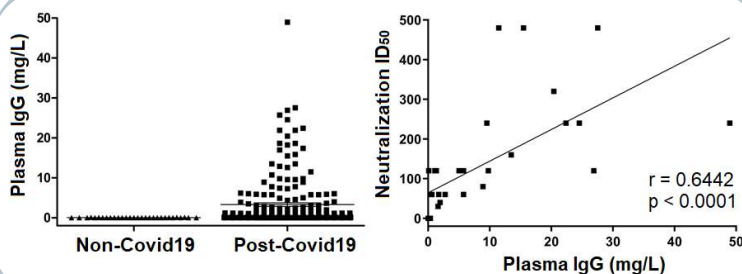
Here, an in-house RBG IgG ELISA test has been validated using a cohort of more than 320 samples of convalescent plasma and serum and adapted to quantify the concentration of plasma RBD IgG and its correlation with the SARS-CoV-2 neutralizing activity *in vitro*.

$r = 0.8884$
$p < 0.0001$
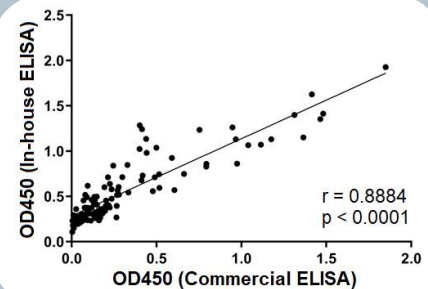
RBD protein from a strain sequenced in the beginning of 2020 was expressed, purified and used in the in-house indirect ELISA to detect anti-RBD specific IgG. The in-house ELISA was validated against a commercial one using 177 plasma samples.

The concentration of RBD IgG (mg/L) in the samples was determined by regression analysis using a standard serially diluted purified commercial IgG.
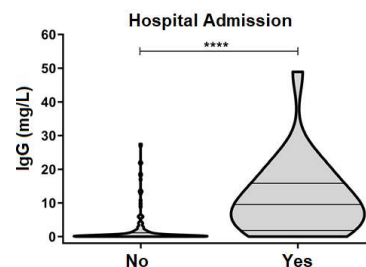
Results

$r = 0.6442$
$p < 0.0001$

Hospital Admission

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The concentration of RBD IgG was found to be significantly higher in the convalescent patients that required hospitalization against the asymptomatic or mild cases.

To calculate plasma or serum viral neutralizing activity (VN), serial dilutions of the samples were incubated with a known concentration of SARS-CoV-2 isolated from a Covid-19 patient, lineage B1.1.

The mixture was added to a monolayer of Vero E6 cells, and the virus-induced cytopathic effect (CPE) observed using crystal violet. The neutralization titer was calculated as the highest serum dilution that protected more than the 50 % of cells from CPE.

There was a high correlation between the concentration of RBD IgG and the VN activity in both plasma and serum.

Conclusions

A quantitative RBD IgG ELISA test has been established and validated in two large cohorts of patients (convalescent plasma and health workers serum samples).

The RBD IgG concentration that predicts the VN activity of convalescent plasma *in vitro* has been determined, and there is correlation between IgG concentration and VN activity.

Furthermore, high concentrations of RBD IgG, and thus, high VN activity are related with higher severity of Covid-19 and the hospitalization of patients.

Establishment of the SARS-CoV-2 RBD IgG concentration in plasma is useful for optimal donor selection and effective passive immunization.

$r = 0.6855$
$p < 0.0001$
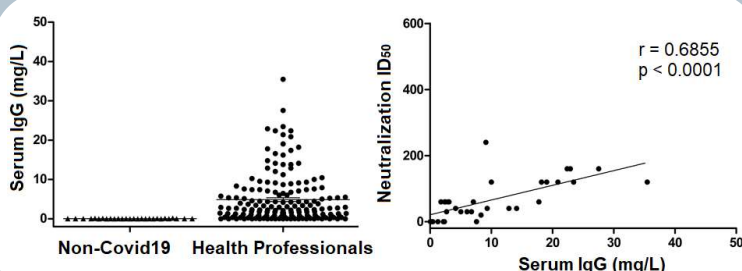
… being a promising criteria for optimization of the efficacy of passive immunization in Covid-19 treatments.