Kinetics of SARS-CoV-2 IgG response: a model from a case report

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Dear Editor,

A few articles describing the temporal trend of the anti-SARS-CoV-2 IgG production, are presently available (1-4) and almost all of these studies deal mainly with the onset of the immune response and neglect the descending phase.

A mathematical model showing the trend and capable, at the same time, to predict it, has not been published yet. In this paper, we tried to model the kinetics of anti SARS-CoV-2 IgG, limited to the descending phase (during the ascending phase, the immunometric assays were not available yet in our Region). The model is based on a single patient, monitored over the time for the specific purpose of studying the immune response. Obviously, it is not possible to provide a statistical approach on a single case, but the result are potentially interesting, since the chosen model presents an excellent goodness-of-fit with the available data.

The subject, an Italian 57-year-old male, living in Pesaro (a province of the Marche Region, one of the main outbreaks of the epidemic in Italy), manifested the onset of symptoms (non-respiratory, but with diarrhea, asthenia, articular and muscle pain, anosmia, and ageusia) starting from March, 9th (fixed as day 0). The duration of the symptoms was 15 days. Health policy, in Italy, at that time, did not allow to perform the swab in the absence of fever, respiratory symptoms and a history of contact with positive subjects.

The blood samples were taken in the days 66, 95, 133 and 224 from the beginning of the symptoms; the immunological test were performed in a clinical laboratory, in Pesaro using a CLIA chemiluminescence assay, (MAGLUMI® SNIBE).

Typical equations of first-order kinetics were used to describe the trend of the IgG concentration, so that a negative exponential function was obtained:

$$C = a\, e^{(-kt)} \quad (1)$$

where t is time (days), C is the serum IgG concentration, k is the elimination constant, a is a constant reflecting the force of the immune response and e is the Euler's number.

Obviously, this approach was possible thanks to the fact that we had to model only the descending phase. With some easy mathematical passages, from (1) we obtain

$$ln\, C = -kt + ln\, a \quad (2)$$

In other words, we find that the logarithm of IgG concentration versus time is linear, so it is possible to apply linear regression methods. Moreover, once we have the equation parameters, it is possible to calculate both the half-life of the specific IgG and the time of their disappearance from the circulation (i.e. the time when the serological test turns negative, <1.1 AU/mL for MAGLUMI® diagnostic assay).

The graph of the exponential model (whose parameters were calculated by linear regression applied to the log-transformed data) is reported in Figure 1. The results show an excellent coefficient of determination (R^2=0.9942). Kinetics parameters for the descending phase of anti SARS-CoV-2 serum IgG concentration are shown in Table 1.

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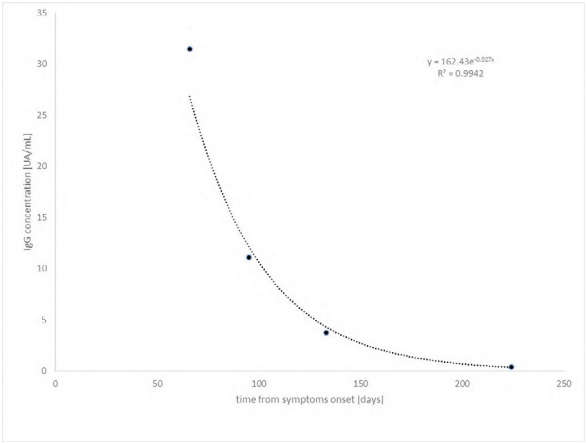

Figure 1
Exponential regression of kinetics data

Table 1
Kinetics parameters for the descending phase of anti-SARS-CoV-2 serum IgG concentration

Parameters	
k	0.027
a	162.43
t(1/2)	25.67 days
t-to-neg	199.98 days

k, elimination constant; a, constant reflecting the force of the immune response; t(1/2), half-life; t-to-neg, time required for the serological test to turn negative.

This result does not necessarily imply a deficiency of immune protection at the expected time of IgG disappearance (i.e. around 6 months, 190 days). Really, as Sette et al. (5) have recently highlighted, a cell-mediated immunity could still be present. Our data become particularly relevant, especially if confirmed on a broader number of patients, since they could be able to give indications about the time required for the serological test to turn negative. The disappearance of IgG antibodies within 6 months (around 190 days) after the onset of symptoms makes the use of antibody testing to infer contact or infection with SARS-CoV-2 more than 6 months previously, very unreliable, or even impossible.

The main limitations of this study are listed below:

- the study was carried on a single patient;
- the patient does not seem to be particularly representative of the COVID-19 positive population (no respiratory symptoms);
- no data on viral load are available;
- the analyzed curve concerns only the descending phase and therefore the IgG peak remains unknown.

Moreover, a huge variability of the IgG kinetics parameters among subjects can be predictable. Nevertheless and despite of the expected inter-subject variability, the good adaptation of the negative exponential model seems to be promising; it also suggests that the model could fit equally well for other cases, with other parameters.

Further studies will be needed to confirm the proposed model, as well as to estimate the variability of the kinetic parameters.

CONFLICT OF INTEREST

None.

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