

## Post-covid-19 immune signatures: Antibody and Th1 cytokine profiles among healthcare workers in Côte d'Ivoire

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### Abstract

The post-SARS-CoV-2 immune response involves both neutralizing antibodies (NAbs) and T-cell cooperation. Healthcare workers, highly exposed in daily practice, represent a relevant population for study. This study aimed to describe the post-COVID-19 immune profiles of Ivorian healthcare workers by analyzing the association between antibodies (IgM, IgG, NAbs) and Th1 cytokines (IL-2, IFN- $\gamma$ , TNF- $\alpha$ ). This cross-sectional study, conducted during January 2022 to June 2023 in three university hospitals in Abidjan, included 36 participants with RT-PCR-confirmed infection. IgM and IgG were measured using an automated analyzer. NAbs were quantified on a multiparametric test system. IL-2, IFN- $\gamma$ , and TNF- $\alpha$  were measured by a flow cytometer. A robust profile was defined by the combined presence of IgG  $\geq$  250 Binding Antibody Units (BAU)/ml, NAbs  $\geq$  800 BAU/ml, and at least one Th1 cytokine (IL-2  $\geq$  2.3 pg/ml or IFN- $\gamma$   $\geq$  0.5 pg/ml). The study participants were 63.9% women with mean age of 40.7 years. All participants had detectable IgG; 69.4% displayed high NAbs, and 75.0% had IL-2  $\geq$  2.3 pg/ml. IgG correlated positively with IL-2 ( $\rho = 0.667$ ;  $p < 0.0001$ ) but negatively correlated with IFN- $\gamma$  ( $\rho = -0.535$ ;  $p = 0.0008$ ). NAbs were positively associated with IL-2 ( $\rho = 0.341$ ;  $p = 0.0416$ ) but negatively associated with IFN- $\gamma$  ( $\rho = -0.740$ ;  $p < 0.0001$ ). Of the participants, 25 (69.4%) were classified as robust and 11 (30.6%) as non-robust. Robust profiles showed higher IgG, NAbs, and IL-2 levels, whereas non-robust profiles had higher IFN- $\gamma$ . Vaccination status did not significantly differentiate groups. In conclusion, in Ivorian healthcare workers, robustness of the post-infection immune response is based on the synergy between NAbs and IL-2. Conversely, high IFN- $\gamma$  levels were associated with weaker neutralization, probably influenced by post-infection kinetics. These results suggested that immune monitoring should integrate combined profiles, beyond IgG alone, to identify individuals requiring priority vaccination follow-up.

**Keywords:** COVID-19; NAbs; IL-2; IFN- $\gamma$ ; post-infection immunity; healthcare workers; Côte d'Ivoire..

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## Introduction

Since the emergence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in late 2019, understanding the mechanisms underlying the adaptive immune response after infection has been critical for preventing severe disease and reinfection. Neutralizing antibodies (Nabs) directed against the viral Spike protein play a central role in protection, as their persistence correlates with a reduced risk of symptomatic infection.<sup>1</sup> Longitudinal studies have shown that these antibodies, along with T-cell responses, can persist for several months after recovery, though their magnitude and duration vary between individuals.<sup>2,3</sup> Protective immunity, however, extends beyond the humoral response. Effective viral control and long-term memory require cooperation between cluster of differentiation (CD)4<sup>+</sup> helper T cells, which promote B-cell activation and the production of high-affinity immunoglobulin G (IgG), and CD8<sup>+</sup> cytotoxic T cells, which eliminate infected cells.<sup>4,5</sup> This coordinated interaction between B and T cells represents a key determinant of durable immunity, as emphasized in recent analyses of both natural infection and vaccination.<sup>6</sup> Comprehensive evaluation of adaptive immunity therefore benefits from the combined assessment of antibodies, immunoglobulin M (IgM), IgG, and Nabs, and T helper 1 (Th1) cytokines, including interleukin-2 (IL-2), interferon-gamma (IFN- $\gamma$ ), and tumor necrosis factor-alpha (TNF- $\alpha$ ). Among these, IL-2 plays a pivotal role by driving T-cell expansion and supporting B-cell differentiation, thus amplifying antibody production.<sup>7,8</sup> IFN- $\gamma$ , a hallmark Th1 cytokine, is essential for antiviral defense, but its overproduction may induce inflammatory responses that do not necessarily enhance neutralization.<sup>9</sup> Such dynamics mirror those described in other respiratory viral infections.<sup>10</sup> In sub-Saharan Africa, and particularly in Côte d'Ivoire, healthcare professionals were among the groups most exposed to SARS-CoV-2, often under limited protective conditions.<sup>11</sup> This makes them a valuable population for investigating the coordination and robustness of post-infection immune responses. In Ghana,

distinct cytokine patterns were already associated with differences in clinical outcomes.<sup>12</sup> Building on this context, the present study aimed to characterize the relationships between antibody markers (IgM, IgG, Nabs) and Th1 cytokines (IL-2, IFN- $\gamma$ , TNF- $\alpha$ ) in Ivorian healthcare workers, in order to identify coordinated and robust immune profiles following SARS-CoV-2 infection.

## Materials and Methods

### *Study design, setting, and period*

This study was part of a multicenter investigation exploring immune responses following SARS-CoV-2 infection among healthcare professionals in Côte d'Ivoire. It was designed as an observational and cross-sectional analysis, conducted between January 2022 and June 2023 in three university hospitals of Abidjan: Cocody, Treichville, and Angré. These institutions were selected for their high patient attendance and the variety of hospital departments, providing diverse exposure conditions for healthcare personnel. The present analysis focused exclusively on baseline samples collected at inclusion (Day 0).

### *Study population and inclusion criteria*

Eligible participants included medical, paramedical, and administrative staff with laboratory-confirmed SARS-CoV-2 infection, diagnosed by reverse transcription quantitative polymerase chain reaction (RT-qPCR), regardless of symptoms presentation at the time of diagnosis. Occupational exposure was categorized as low, intermediate or high depending on the work environment and frequency of contact with suspected or confirmed COVID-19 patients. The study enrolled 36 participants, met the inclusion criteria. Sociodemographic and clinical information were collected using a structured questionnaire at inclusion.

### *Sampling procedures*

From each participant, 5 ml of venous blood was collected on ethylenediaminetetraacetic acid (EDTA) and another 5 ml on a dry tube. A nasopharyngeal swab was also obtained for

molecular confirmation. All biological samples were processed within two hours after collection. Serum and plasma aliquots were stored at -80 °C until analysis, avoiding repeated freeze-thaw cycles.

#### *Laboratory analyses*

- Molecular confirmation (RT-qPCR)

Detection of SARS-CoV-2 RNA was performed on nasopharyngeal swabs transported in viral transport medium at 2-8 °C. RNA extraction was carried out using the King Fisher™ Duo Prime automated platform (Thermo Fisher Scientific, Waltham, MA, USA) with the MagMAX™ Viral/Pathogen kit. Amplification was done on a CFX96™ Real-Time PCR Detection System (Bio-Rad, Hercules, CA, USA), targeting the nucleocapsid (N) and RNA-dependent RNA polymerase (RdRp) genes. A cycle threshold (Ct) value < 35 indicated positivity. Each analytical series included an internal control, a certified positive control, and a negative control to ensure assay validity.

- Serological assays (IgM and IgG anti-RBD)

Specific antibodies directed against the receptor-binding domain (RBD) of the Spike protein were quantified using the Mini-VIDAS® analyzer (Serial No. IVD7006414, Ref. 410417, BioMérieux SA, Marcy-l'Étoile, France). The VIDAS® SARS-CoV-2 IgM and VIDAS® SARS-CoV-2 IgG II kits are based on enzyme-linked fluorescent assay (ELFA) technology. Results were standardized according to the 1st WHO International Standard (20/136)<sup>13</sup> and expressed in Binding Antibody Units per milliliter (BAU/ml). Samples with index values ≥ 1.0 were considered positive; concentrations ≥ 20 BAU/ml indicated seropositivity, and IgG ≥ 250 BAU/mL defined a strong humoral response.

- Neutralizing antibody quantification

NAbs targeting the S1 subunit of the Spike protein were quantified using the CHORUS TRIO® semi-automated system (Serial No. 4341, P/N 81200; Diesse Diagnostica Senese S.p.A., Siena, Italy) and the CHORUS SARS-CoV-2 “Neutralizing” Ab kit. The method is a competitive enzyme immunoassay, in which antibodies in the sample compete with labeled

tracers for binding to the viral RBD/angiotensin-converting enzyme 2 (ACE2) complex. The degree of inhibition reflects functional neutralization capacity and was expressed in BAU/ml, aligned with WHO standard 20/136.<sup>13</sup> Interpretation thresholds were as follows: < 20 BAU/ml (negative), 20-49.9 BAU/ml (equivocal), and ≥ 50 BAU/ml (positive). Each run included internal quality controls and a certified calibration curve to ensure analytical reproducibility.

- Cytokine profiling

Cytokine quantification focused on three Th1-type mediators: interleukin-2 (IL-2), interferon-gamma (IFN-  $\gamma$ ), and tumor necrosis factor-alpha (TNF- $\alpha$ ). Measurements were performed on plasma using the BD™ Cytometric Bead Array (CBA) Human Th1/Th2/Th17 Kit (Ref. 560484; BD Biosciences, San Jose, CA, USA). Acquisition was carried out on a flow cytometer (Serial No. V3389002039; BD FACSCanto™ II flow cytometer), and analysis was conducted with FCAP Array™ v3.0 software (BD Biosciences). Plasma samples were centrifuged within one hour of collection at 1500-2000  $\times$  g, for 10 min, before freezing.

- Definition of analytical thresholds

Functional thresholds were established from literature benchmarks and the empirical distribution observed in this cohort. A strong humoral response was defined as IgG ≥ 250 BAU/ml. A recent or moderate seroconversion was defined by IgM ≥ 30 BAU/ml. A high neutralizing capacity corresponded to NAb ≥ 800 BAU/ml, a range associated with efficient viral neutralization in prior studies.<sup>1</sup> Th1 cytokine activation was indicated by IL-2 ≥ 2.3 pg/ml, IFN-  $\gamma$  ≥ 0.5 pg/ml, or TNF- $\alpha$  ≥ 3.0 pg/ml.

Participants were categorized according to an integrated immune phenotype: a robust profile combined both strong humoral markers (IgG ≥ 250 BAU/ml and NAb ≥ 800 BAU/ml) and at least one sign of Th1 activation (IL-2 ≥ 2.3 pg/ml or IFN-  $\gamma$  ≥ 0.5 pg/ml). Profiles lacking one or more of these components were classified as non-robust. This operational definition was developed to capture the functional

coordination of antibody- and cytokine-mediated immunity.

#### Statistical Analysis

Data were processed and analyzed using the Statistical Package for the Social Sciences (SPSS) v26.0 (IBM Corp., Armonk, NY, USA). Quantitative variables were presented as means  $\pm$  standard deviation (SD) or medians (interquartile range, IQR), depending on normality. Categorical variables were expressed as frequencies and percentages. Associations between antibody titers (IgG, NAbs) and cytokines (IL-2, IFN- $\gamma$ , TNF- $\alpha$ ) were examined using the Spearman's rank correlation coefficient ( $\rho$ ). Differences between robust and non-robust profiles were evaluated using the Mann-Whitney U test for continuous variables and the Chi-square or Fisher's exact test for categorical variables. Statistical significance was set at  $p < 0.05$ .

## Results

### General characteristics of participants

Among the 36 healthcare workers included, 63.9% were women. The mean age was  $40.7 \pm$

12.8 years, and the mean body mass index (BMI) was  $26.0 \pm 4.3 \text{ kg/m}^2$ . Half of the participants worked at the University Hospital of Cocody (50.0%), 30.6% at Angré, and 19.4% at Treichville. The most represented professionals were nurses (30.6%) and physicians (27.8%). The majority was assigned to emergency units (50.0%), and occupational risk was assessed as intermediate or high in 83.3%. For preventive measures, 35 participants (97.2%) reported using personal protective equipment (PPE); nonetheless, one-third of healthcare workers perceived its effectiveness as limited. The history of COVID-19 infection was reported by 38.9%. At enrollment, 52.8% were symptomatic. Medical histories (notably cardio-metabolic and atopic conditions) were present in 44.4%. Work-related stress was declared by 55.6%. Regarding vaccination, 30/36 (83.3%) of the participants had received at least one dose prior to the index infection. Among the vaccinated ( $n = 30$ ), most received an mRNA vaccine (56.7%) or a viral-vector vaccine (40.0%); 80.0% had received two doses, with a mean interval of  $1.6 \pm 1.1$  months between the last dose and sampling (Table 1).

**Table 1.** General characteristics of the 36 healthcare workers included in the study.

Variable	Categories	n (%)
Sex	Female / Male	23 (63.9) / 13 (36.1)
Age (years)	Mean $\pm$ SD	$40.7 \pm 12.8$
BMI ( $\text{kg/m}^2$ )	Mean $\pm$ SD	$26.0 \pm 4.3$
Hospital site	Cocody / Angré / Treichville	18 (50.0) / 11 (30.6) / 7 (19.4)
Occupational risk level	Low / Intermediate / High	6 (16.7) / 17 (47.2) / 13 (36.1)
Use of PPE	Yes	35 (97.2)
Perceived PPE effectiveness	Effective / Relative	24 (66.7) / 12 (33.3)
Clinical status at enrollment	Asymptomatic / Symptomatic	17 (47.2) / 19 (52.8)
Medical history	None / Present	20 (55.6) / 16 (44.4)
Reported stress	Yes	20 (55.6)
Vaccinated	Yes / No	30 (83.3) / 6 (16.7)
Number of doses received	1 / 2	6 (20.0) / 24 (80.0)*
Type of vaccine	mRNA / Viral vector / Heterologous	(56.7) / 12 (40.0) / 1 (3.3)*

\*Calculated among vaccinated only ( $n = 30$ ). BMI = body mass index; UH = University Hospital; PPE = Personal Protective Equipment.

*Humoral and cytokine responses at baseline (Day 0)*

At baseline, median levels were as follows: IgM 36.4 BAU/ml [22.8-79.3], IgG 556.3 BAU/ml [458.7-662.3] and NAbs 1469.6 BAU/ml [788.8-

1547.2]. For Th1 cytokines, median concentrations were IL-2 2.5 pg/ml [2.1-2.6], IFN-  $\gamma$  0.38 pg/ml [0.22-1.34], and TNF- $\alpha$  2.9 pg/ml [1.65-5.82] (Table 2).

**Table 2.** Baseline of humoral and Th1 cytokine levels among healthcare workers (Day 0).

Marker	Median (50%)	[Q1 - Q3] (IQR)	Min	Max
IgM (BAU/ml)	36.41	[22.77 - 79.27]	10.53	106.79
IgG (BAU/ml)	556.31	[458.68 - 662.26]	258.17	776.75
NAbs (BAU/ml)	1469.60	[788.80 - 1547.20]	45.20	1732.30
IL-2 (pg/ml)	2.48	[2.14 - 2.59]	1.00	3.00
IFN- $\gamma$ (pg/ml)	0.38	[0.22 - 1.34]	0.10	2.14
TNF- $\alpha$ (pg/ml)	2.94	[1.65 - 5.82]	1.34	6.40

Values are expressed as median [interquartile range]. Units: antibodies in BAU/ml; cytokines in pg/ml.

NAbs = neutralizing antibodies; IL = interleukin; IFN = interferon; TNF = tumor necrosis factor.

*Correlations between humoral responses and Th1 cytokines*

IgG levels were strongly and positively correlated with IL-2 ( $\rho = 0.667$ ;  $p < 0.0001$ ), but negatively correlated with IFN-  $\gamma$  ( $\rho = -0.535$ ;  $p = 0.0008$ ). NAbs were positively associated with

IL-2 ( $\rho = 0.341$ ;  $p = 0.0416$ ) and negatively correlated with IFN-  $\gamma$  ( $\rho = -0.740$ ;  $p < 0.0001$ ). The correlation between IgG and NAbs was positive but did not reach statistical significance ( $\rho = 0.273$ ;  $p = 0.1069$ ) (Table 3).

**Table 3.** Spearman's rank correlations between antibody levels and Th1 cytokine concentrations at baseline (Day 0).

Correlations	Spearman's rho	p-value
IgG vs IL-2	0.667	<0.0001
IgG vs IFN- $\gamma$	-0.535	0.0008
NAbs vs IL-2	0.341	0.0416
NAbs vs IFN- $\gamma$	-0.740	<0.0001
IgG vs NAbs	0.273	NS

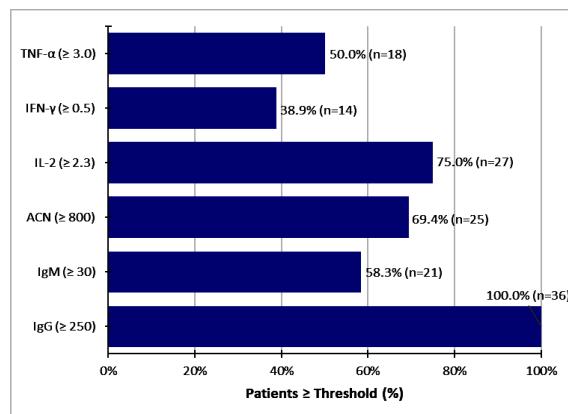
$\rho$  = Spearman's correlation coefficient.  $p > 0.05$  is not significant (NS). IgG = immunoglobulin G;

NAbs = neutralizing antibodies; IL = interleukin; IFN = interferon.

*Distribution of immune markers according to functional thresholds*

All participants had IgG  $\geq 250$  BAU/ml (100%). In contrast, 58.3% had IgM  $\geq 30$  BAU/ml 69.4%

had NAbs  $\geq 800$  BAU/ml, and 75.0% showed IL-2  $\geq 2.3$  pg/ml. Elevated IFN-  $\gamma$  ( $\geq 0.5$  pg/ml) was observed in 38.9% of participants, and TNF- $\alpha$   $\geq 3.0$  pg/ml in 50.0% (Figure 1).



**Figure 1.** Distribution of immune markers above functional thresholds among the 36 healthcare workers with prior SARS-CoV-2 infection. Bars indicate the proportion of participants with antibody or cytokine levels equal to or greater than the defined cutoffs: IgG  $\geq 250$  BAU/ml, IgM  $\geq 30$  BAU/ml, NAbs  $\geq 800$  BAU/ml, IL-2  $\geq 2.3$  pg/ml, IFN- $\gamma$   $\geq 0.5$  pg/ml, and TNF- $\alpha$   $\geq 3.0$  pg/ml.

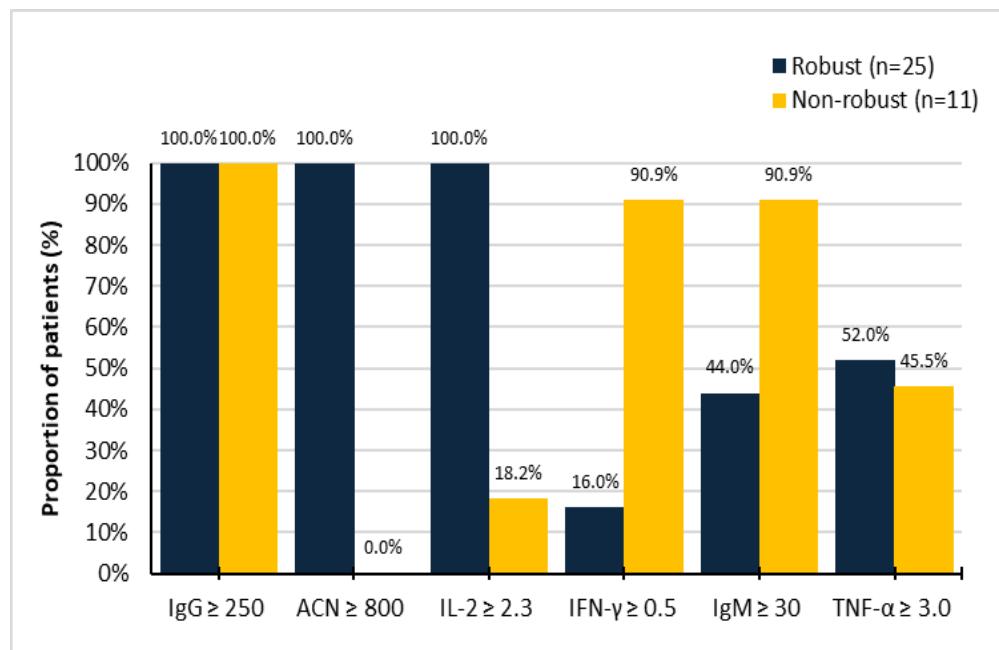
### Comparison of robust vs non-robust profiles

Based on our definition, 25/36 participants (69.4%) were classified as robust and 11/36 (30.6%) as non-robust. As expected, all robust profiles displayed NAbs  $\geq 800$  BAU/ml and IL-2  $\geq 2.3$  pg/ml. Quantitatively, robust profiles had higher IgG (628 vs. 451 BAU/ml,  $p = 0.013$ ), NAbs (1547 vs. 465 BAU/ml,  $p < 0.001$ ), and IL-2 (2.5 vs. 1.1 pg/ml,  $p < 0.001$ ). Conversely, non-robust participants exhibited higher IFN- $\gamma$  levels (2.1 pg/ml vs. 0.4 pg/ml,  $p < 0.001$ ). No significant differences were observed between groups for IgM, TNF- $\alpha$ , age, sex, hospital site, clinical presentation, medical history, stress, or vaccination status (all  $p > 0.05$ ) (Table 4, Figure 2).

**Table 4.** Comparison of clinical, vaccination, and immunological characteristics between robust and non-robust profiles in the 36 participants at Day 0.

Variable	Robust (n = 25)	Non-robust (n = 11)	p-value
Age (years)	39.0 [28.0-56.0]	37.0 [31.5-45.0]	NS
Number of vaccine doses	2.0 [1.0-2.0]	2.0 [1.5-2.0]	NS
Infection-to-sampling interval (months)	0.0 [0.0-13.0]	0.0 [0.0-1.0]	NS
Vaccination-to-sampling interval (months)	5.0 [3.0-11.0]	5.0 [4.5-8.5]	NS
IgM (BAU/ml)	24.8 [21.8-66.9]	70.0 [50.1-86.6]	NS
IgG (BAU/ml)	628.0 [543.5-710.5]	451.0 [351.0-551.0]	0.013
NAbs (BAU/ml)	1547.0 [1469.0-1732.0]	465.0 [45.0-812.0]	<0.001
IL-2 (pg/ml)	2.5 [2.3-2.8]	1.1 [0.7-2.1]	<0.001
IFN- $\gamma$ (pg/ml)	0.4 [0.3-0.5]	2.1 [1.6-2.4]	<0.001
TNF- $\alpha$ (pg/ml)	2.9 [2.3-3.4]	2.5 [1.5-3.3]	NS
Female sex (%)	16 (64.0)	7 (63.6)	NS
Hospital site (UH-Cocody)	13 (52.0)	5 (45.5)	NS
Symptomatic status (%)	12 (48.0)	7 (63.6)	NS
Medical history (%)	10 (40.0)	5 (45.5)	NS
Reported stress (%)	14 (56.0)	6 (54.5)	NS
Vaccinated (%)	22 (88.0)	8 (72.7)	NS
mRNA vaccine (%)	12 (48.0)	5 (45.5)	NS

Values are expressed as median [interquartile range] or frequency (percentage). Continuous variables were compared using the Mann-Whitney U test; categorical variables with the  $\chi^2$  test or Fisher's exact test.  $p > 0.05$  is not significant (NS). NAbs = neutralizing antibodies; UH = University Hospital.



**Figure 2.** Comparison of immune marker distribution between robust and non-robust immune profiles. Bars represent the proportion of participants within each subgroup meeting the functional thresholds for humoral (IgM, IgG, NAbs) and Th1 cytokine (IL-2, IFN- $\gamma$ , TNF- $\alpha$ ) responses. Robust profiles (n = 25) combined strong humoral and Th1 activation (IgG  $\geq 250$  BAU/ml, NAbs  $\geq 800$  BAU/ml, IL-2  $\geq 2.3$  pg/ml). Non-robust profiles (n = 11) lacked one or more of these criteria.

## Discussion

Our study showed that beyond the near-universal IgG seropositivity, the quality of the post-SARS-CoV-2 immune response relied on the coordination between humoral and cellular arms. The strong positive correlation between IgG and IL-2 ( $\rho = 0.667$ ;  $p < 0.0001$ ) highlighted this functional cooperation between CD4 $^{+}$  T helper and B lymphocytes. IL-2 drives T-cell clonal expansion and B-cell differentiation into IgG-secreting plasma cells, thereby sustaining higher antibody titers.<sup>7,8</sup> In our cohort, participants with robust profiles exhibited concurrent elevations of IgG and IL-2, supporting this mechanism. These observations reinforce the concept proposed by Sette & Crotty, 2021, and Grifoni et al., 2020,<sup>4,5</sup> emphasizing that efficient T and B cells cooperation underpins durable and coordinated immune memory.

A striking feature of our findings was the negative correlation between NAbs and IFN- $\gamma$  ( $\rho = -0.740$ ;  $p < 0.0001$ ). Participants with non-robust profiles exhibited higher IFN- $\gamma$

concentrations (2.1 vs. 0.4 pg/ml,  $p < 0.001$ ), suggesting that intense cytotoxic and inflammatory responses do not necessarily correspond to superior neutralization capacity. Similar trends were reported by Garcia-Beltran et al., 2021,<sup>14</sup> where excessive inflammatory activation was associated with weaker protective humoral immunity. Although IFN- $\gamma$  remains essential for viral control and vaccine efficacy, exaggerated Th1 polarization may reflect an early or dysregulated response. In our study, heterogeneity in infection-to-sampling intervals (0-13 months) likely contributed to this pattern, with elevated IFN- $\gamma$  marking more recent infections rather than a true antagonism between inflammation and antibody quality.

By combining high IgG and NAbs titers with evidence of Th1 activation, we identified two subpopulations: robust (69.4%) and non-robust (30.6%). Robust profiles displayed markedly higher NAbs concentrations (1547 BAU/ml vs. 465 BAU/ml,  $p < 0.001$ ) and IL-2 activity, whereas non-robust participants showed polarization toward IFN- $\gamma$ . This integrated approach, assessing humoral and cellular

biomarkers together, provided a more functional perspective than isolated measurements. While neutralization remains a core correlate of protection,<sup>15</sup> its interpretation gains precision when considered in the context of a balanced Th1 cytokine environment, as also discussed by Gruell et al., 2022.<sup>16</sup> Such composite profiling could help identify individuals with suboptimal coordination of immune mechanisms.

Vaccination status did not significantly influence the classification into robust or non-robust profiles ( $p > 0.05$ ). This may reflect both the small sample size ( $n = 36$ ) and the prevalence of hybrid immunity, combining natural infection and vaccination, which is known to homogenize and enhance antibody responses.<sup>17</sup> The relatively narrow dispersion of IgG values observed across participants supports this hypothesis. Hybrid immunity likely contributed to the high overall seropositivity and the reduced variability in antibody titers within this highly exposed population.

Our data suggested that post-infection immune evaluation limited to IgG serology may overlook key differences in immune quality. Including NAbs and Th1 cytokines such as IL-2 and IFN- $\gamma$  allows better discrimination between robust and non-robust responders. In Côte d'Ivoire and other sub-Saharan contexts, such integrated immunomonitoring could guide the prioritization of healthcare workers for booster vaccination or closer surveillance, particularly those in emergency and critical-care settings with sustained exposure risk.

This study has several limitations. The limited sample size ( $n = 36$ ) restricted statistical power and prevented multivariable adjustment. The wide variability in infection-to-sampling intervals (0-13 months) may have affected antibody and cytokine kinetics, particularly for IFN- $\gamma$ . The inclusion of only Ivorian healthcare workers could also limit generalizability. Finally, the operational definition of the "robust profile" and the thresholds used remain exploratory and require validation in larger longitudinal cohorts.

In conclusion, this study demonstrated that among Ivorian healthcare workers with RT-PCR-confirmed SARS-CoV-2 infection, the robustness

of post-infection immunity depends primarily on the coordination between neutralizing antibodies and Th1 cytokines, particularly IL-2. Conversely, elevated IFN- $\gamma$  levels were associated with weaker neutralization, likely reflecting post-infection immune kinetics rather than impaired protection. These findings support the use of integrated immune profiling, combining humoral and cellular markers, to move beyond IgG serology alone. Identifying non-robust immune profiles may help optimize booster vaccination strategies and occupational surveillance.

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## Author Contributions

APVG: conceptualized and designed the study, performed the investigation and data analysis, and drafted the manuscript. SRD: supervised the study, coordinated the project, secured funding, and reviewed the manuscript. AHA; ORY; AUAA; NSM: performed laboratory work and collected data. YJS; ATEA; BDYFO: performed data curation, validation, and provided technical support. KN; KLS: supervised the study. All authors participated in writing and reviewing the paper and approved the final version.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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## Ethical approval

The study protocol was reviewed and approved by the National Ethics Committee for Life Sciences and

Health (CNESVS) of Côte d'Ivoire (Ref. 007-22/MSHP/CMU/CNESVS-km).

## Informed consent

A written informed consent was obtained from each participant prior to inclusion in the study.

## References

1. Khoury, D.S., Cromer, D., Reynaldi, A., et al. (2021). Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med.* 27:1205-11.
2. Tan, Y., Liu, F., Xu, X., et al. (2020). Durability of neutralizing antibodies and T-cell response post SARS-CoV-2 infection. *Front Med.* 14(6):746-51.
3. Dan, J.M., Mateus, J., Kato, Y., et al. (2021). Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. *Science.* 371(6529):eabf4063.
4. Sette, A., Crotty, S. (2021). Adaptive immunity to SARS-CoV-2 and COVID-19. *Cell.* 184(4):861-80.
5. Grifoni, A., Weiskopf, D., Ramirez, S.I., et al. (2020). Targets of T cell responses to SARS-CoV-2 coronavirus in humans with COVID-19 disease and unexposed individuals. *Cell.* 181(7):1489-501.e15.
6. Upreti, S., Samant, M. (2022). A review on immunological responses to SARS-CoV-2 and various COVID-19 vaccine regimens. *Pharm Res.* 39(9):2119-34.
7. Mingari, M.C., Gerosa, F., Carra, G., et al. (1984). Human interleukin-2 promotes proliferation of activated B cells via surface receptors similar to those of activated T cells. *Nature.* 312(5995):641-3.
8. Cohen, K.W., Linderman, S.L., Moodie, Z., et al. (2021). Longitudinal analysis shows durable and broad immune memory after SARS-CoV-2 infection with persisting antibody responses and memory B and T cells. *Cell Rep Med.* 2(7):100354.
9. Guo, L., Wang, G., Wang, Y., et al. (2022). SARS-CoV-2-specific antibody and T-cell responses 1 year after infection in people recovered from COVID-19: a longitudinal cohort study. *Lancet Microbe.* 3(5):e348-56.
10. Siggins, M.K., Thwaites, R.S., Openshaw, P.J.M. (2021). Durability of immunity to SARS-CoV-2 and other respiratory viruses. *Trends Microbiol.* 29(7):648-62.
11. Kouadio, Y.J., Konan, K.J., N'Guessan, K., et al. (2022). COVID-19 et exposition des soignants en Afrique de l'Ouest: défis et perspectives. *Rev Santé Publique.* 34(2):145-52.
12. Tapela, K., Oyawoye, F.O., Olwal, C.O., et al. (2022). Probing SARS-CoV-2-positive plasma to identify potential factors correlating with mild COVID-19 in Ghana, West Africa. *BMC Med.* 20(1):370.
13. World Health Organization. First WHO International Standard for anti-SARS-CoV-2 immunoglobulin (human). National Institute for Biological Standards and Control (NIBSC), code 20/136. Instructions for use, version 2.0. London (UK); 2020. Available at: <https://nibsc.org/documents/ifu/20-136.pdf>. Accessed on: 3 January 2026.
14. Garcia-Beltran, W.F., Lam, E.C., Astudillo, M.G., et al. (2021). COVID-19-neutralizing antibodies predict disease severity and survival. *Cell.* 184(2):476-88.e11.
15. Tea, F., Ospina Stella, A., Aggarwal, A., et al. (2021). SARS-CoV-2 neutralizing antibodies: longevity, breadth, and evasion by emerging viral variants. *PLoS Med.* 18(7):e1003656.
16. Gruell, H., Vanshylla, K., Weber, T., et al. (2022). Antibody-mediated neutralization of SARS-CoV-2. *Immunity.* 55(6):925-44.
17. Suryawanshi, R., Ott, M. (2022). SARS-CoV-2 hybrid immunity: silver bullet or silver lining? *Nat Rev Immunol.* 22(10):591-2.