Research Article

Routine use of SARS-CoV-2 IgM and IgG Antibodies: A Practical Approach in Gabon

Berthe Amélie Iroungou[1*], Arnaud Nze Ossima[2], Annicet Clotaire Dikoumba[1], Aurore Prislya Bouassa Bouassa[1], Guignali Laurette Mangouka[3]

Abstract

Background: In late 2019, a novel coronavirus initiated a global pandemic, raising worldwide concerns. As mass screening decreased, testing waned, leading the WHO to declare the COVID-19 emergency over in May 2023. This study presents findings on the application of a serological Point of Care system for diagnosing, monitoring, and surveilling COVID-19 in at-risk individuals within a hospital setting.

Methods: This cross-sectional retrospective study included serological immuno-fluorescent tests for immunoglobulin M (IgM) and immunoglobulin G (IgG) on samples from 742 individuals admitted to the Military Hospital (HIAOBO), encompassing healthcare workers and their families, vaccinated individuals, and persons recovered from COVID-19 between October 2021 and July 2022.

Results: The study included 742 participants, predominantly female (52%), with an average age of 41.37 ± 14.62 years, and 55% were healthcare workers. The overall seroprevalence of IgM and IgG was 313 (42.18%) and 369 (49.73%), respectively. Among symptomatic cases, 54.05% tested positive for IgM and 69.73% for IgG. IgM and IgG were detected in 40.27% and 51.01% of HIV-infected patients, respectively, and in 37.50% and 40.20% of healthcare workers and their families.

Conclusions: This study underscores the critical role of serological testing in understanding diverse immune responses. The findings offer valuable insights for developing tailored strategies for COVID-19 management.

Keywords: COVID-19; IgM; IgG; Immune response; Gabon

Introduction

In late December 2019, the world was thrust into a state of high alert due to the emergence of a novel coronavirus, leading to severe acute respiratory syndrome (SARS-CoV-2). This prompted the immediate mobilization of healthcare systems worldwide. Originating in Wuhan, Hubei province, China, the virus rapidly disseminated globally through human migration, ultimately evolving into a full-fledged pandemic [1].

On May 5, 2023, the Director-General of the World Health Organization (WHO) expressed cautious optimism by declaring the end of the public health emergency related to COVID-19. However, it is crucial to note that this declaration does not imply that the disease is no longer a global threat. Post-acute sequelae of SARS-CoV-2 infection (PASC), commonly known as long COVID, remains a significant concern, with over 30% of adult patients

Affiliation:

[1]Unité Mixte de Recherche CIRMF-SSM, Libreville, Gabon

[2]AP-HP Health Economics, Research Unit, Hotel Dieu Hospital, Paris

[3]Service de Médecine Interne, Hôpital d'Instruction des Armées Omar Bongo Ondimba, Libreville, Gabon

*Corresponding author:
Berthe Amélie Iroungou, Unité Mixte de Recherche CIRMF-SSM, Libreville, Gabon.

experiencing symptoms at 1-2 months and 10-15% at 6-8 months post-infection. This underscores the necessity for biological diagnosis when PCR testing is not feasible [2]. In Gabon, the government discontinued mass screening via PCR and antigen testing on April 14, 2022. During the pandemic, the strategy primarily focused on PCR, with serology being rarely utilized. However, due to the cost and limited availability of reagents and consumables, routine COVID-19 diagnosis became challenging. Given the prevalence of long COVID and the limitations of PCR sensitivity post-pandemic, it is imperative that developing countries consider the routine use of serology tests for viral infections to support their health system [3]. These tests detect the presence of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies in individuals exposed to the infection 7 to 14 days prior.

The detection of antibodies is crucial for understanding the seroprevalence of SARS-CoV-2, comprehending the global dynamics of the ongoing COVID-19 pandemic, and estimating the prevalence of unreported SARS-CoV-2 infections [4,5]. It is of paramount importance to propose effective solutions to government authorities for preventing and monitoring COVID-19. While the PCR test remains the primary diagnostic method, Point-of-Care serology should be seriously considered as a cost-effective alternative Ondo A. Gabon : Le coût réel d'un test au Covid-19 est de 300 000 FCFA [Internet]. La Libreville. 2021 [cited 2023 Nov 1]. Available from: https://lalibreville.com/gabon-le-cout-reel-dun-test-au-covid-19-est-de-300-000-fcfa/. Therefore, in this study, we present insights on the application of a serological Point-of-Care system for the diagnosis, monitoring, and surveillance of COVID-19 within a hospital setting. This study focuses on healthcare workers and their families, hospitalized patients, and individuals living with HIV. While our results may not be more significant than other studies on serology tests, we aim to demonstrate how serology was effectively integrated into our healthcare system.

Materials and Methods

Study Design and Setting

This cross-sectional retrospective study was conducted to evaluate serological immuno-fluorescent tests for immunoglobulin M (IgM) and immunoglobulin G (IgG) in individuals admitted to the Military Hospital (HIAOBO). The study population included healthcare workers and their families, vaccinated individuals, and persons who had recovered from COVID-19. The study period spanned from October 2021 to July 2022.

Our unit primarily focuses on the follow-up of persons living with HIV. Despite restrictions during the pandemic, these individuals continued to frequent the hospital for care.

Consequently, our unit became a reference center for SARS-CoV-2 virus diagnosis during this time. The inclusion of this diverse patient population allowed for a comprehensive assessment of serological responses across different groups, enhancing the generalizability and relevance of our study outcomes.

Study Population

The study recruited participants from three distinct groups spanning various generations: Group I comprised individuals living with HIV without a history of SARS-CoV-2 infection, Group II consisted of healthcare workers and their families, regardless of their COVID-19 status, and Group III included patients admitted to the intensive care unit (ICU) with clinically diagnosed COVID-19 confirmed by RT-PCR-positive tests.

Exclusion criteria encompassed individuals who believed they had acquired immunity post-COVID-19 and vaccinated patients, ensuring a focused analysis of serological responses in unvaccinated and previously uninfected individuals. This approach allowed for clearer insights into the natural immune response to SARS-CoV-2 across different demographic groups.
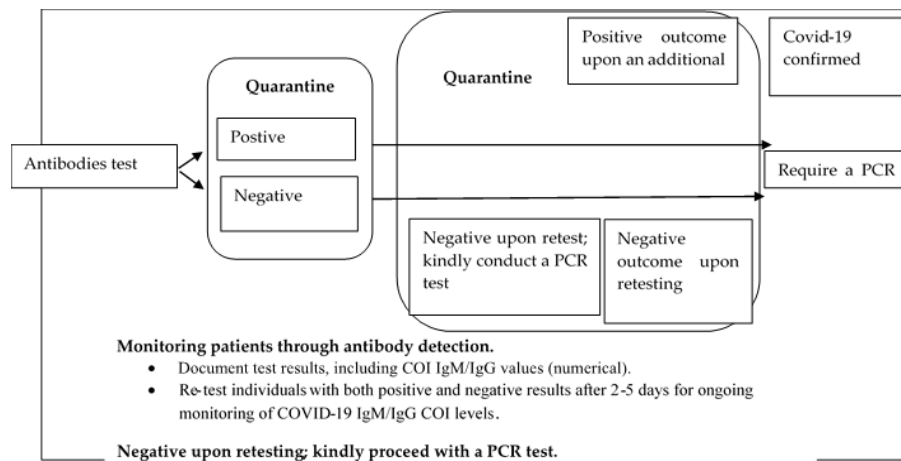
Data Collection *(Figure 1: Antibody Detection Protocol)*

Serum samples from the study populations were collected in 1.5 mL EDTA tubes and subsequently centrifuged at 3000 g for 10 minutes. Post-centrifugation, serology tests were promptly conducted using an in vitro diagnostic system based on lateral flow sandwich detection immunofluorescence technology. This system targeted anti-SARS-CoV-2 IgM and IgG antibodies and employed Ichroma II COVID-19 Ab kits along with the Ichroma II Reader from Boditech Med Inc., South Korea (Figure 1). All tests were performed in strict adherence to the manufacturer's instructions.

The Ichroma II COVID-19 Ab test, read on the Ichroma II Reader, exhibited a sensitivity of 95.8% and a specificity of 97%. The IgG and IgM kits utilized a cut-off index of 0.9, where values greater than 0.9 were considered reactive (positive), and those less than or equal to 0.9 were classified as nonreactive (negative) [6].

By ensuring rigorous adherence to the established protocol, the study aimed to provide accurate and reliable serological data for the assessment of SARS-CoV-2 antibody prevalence and immune response within the study populations.

Immunoglobulin M (IgM), Immunoglobulin G(IgG), COI (cutoff (COI). COI <1.0 is negative for anti-SARS-CoV-2 antibodies, COI=1 is considered intermediate and COI >1.0 is considered positive.

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Figure 1: Antibody Detection Protocol.

Variables and Outcome

Sociodemographic characteristics, including age and gender, were measured, and the primary outcome was the level of IgG and IgM against SARS-CoV-2, determined by serum samples collected from the patients.

Statistical Analysis

Descriptive statistics were provided using mean, standard deviation, interquartile range, median, minimum, and maximum values for continuous variables, and frequencies and percentages for categorical variables. Group differences were assessed using Chi-square tests for categorical variables. For quantitative variables, either a student's t-test or Wilcoxon Mann-Whitney test was employed based on the distribution characteristics. The outcome variables were the positive or negative serostatus of IgG and IgM. A 2 × 2 table was generated to compare IgM and IgG antibodies, and the quantitative correlation between IgM and IgG was evaluated using Pearson correlation. Cross tabulations were performed against the gender variable. P-values below 0.05 were considered statistically significant. All statistical tests were two-sided. Statistical analyses were performed using R statistical software version 4.1.3 (https://www.r-project.org).

Ethical Consideration

This study was conducted in accordance with the ethical guidelines outlined in the Declaration of Helsinki 1995 (revised in 2013). It received approval from the National Ethics Committee for Research under reference number PROT N°0017/2020/PR/SG/CNER.

Results

Characteristics of Population

We analyzed 742 eligible individuals (Figure 2) from a total population of 815, excluding those who believed they had acquired immunity post-COVID-19 and vaccinated patients. Participant characteristics are presented in Table 1. The average age (mean±standard deviation) was 41.37 ± 14.62 years, 52% were female, and 55% were healthcare workers and their families.

Characteristics of Population

Among the 742 eligible participants, 185 (25%) were symptomatic cases with a mean age of 43.33 ± 15.07 years, of which 35% were female. Healthcare workers and their families comprised 408 (55%) of the participants, with a mean age of 40.15 ± 14.91 years, and 54% were female. The remaining 149 (20%) participants were HIV-infected individuals, with a mean age of 42.30 ± 12.92 years, and 68% were female.

Serology Testing

Overall, 42.18% of the participants tested positive for IgM, indicating an active or recent infection, while 49.73% tested positive for IgG, indicating a past infection. Regarding the stages of infection, 15.77% were in the first phase, 23.32% in the second stage, and 26.42% were in both stages, indicating a recent infection that may still be contagious. Additionally, 34.50% of individuals demonstrated an immune response (Table 1).

The seroprevalence of IgG and IgM across the groups is summarized in Table 1. Among symptomatic cases, 54.05% tested positive for IgM and 69.73% for IgG. In the HIV-infected group, 40.27% were positive for IgM and 51.01% for IgG. Among healthcare workers and their families, 37.50% tested positive for IgM and 40.20% for IgG. The proportion of symptomatic cases positive for both IgM and IgG (IgM+IgG+: 44.86%) was higher than that of HIV-infected

patients (IgM+IgG+: 24.83%) and healthcare workers and their families (IgM+IgG+: 18.63%).

The Spearman correlation test revealed a significant association between IgM and IgG levels in symptomatic cases, patients living with HIV, and healthcare workers and their families, with p-values < 0.05 and correlation coefficients of 0.37, 0.25, and 0.23, respectively.

Comparison of Immune Response Between People Living with HIV and Hospitalized Patients

We examined the immune response in two distinct groups: individuals living with HIV and patients hospitalized for specific investigations, aiming to identify potential variations in their respective immunological reactions (Table 2). A significant gender distribution difference was noted,
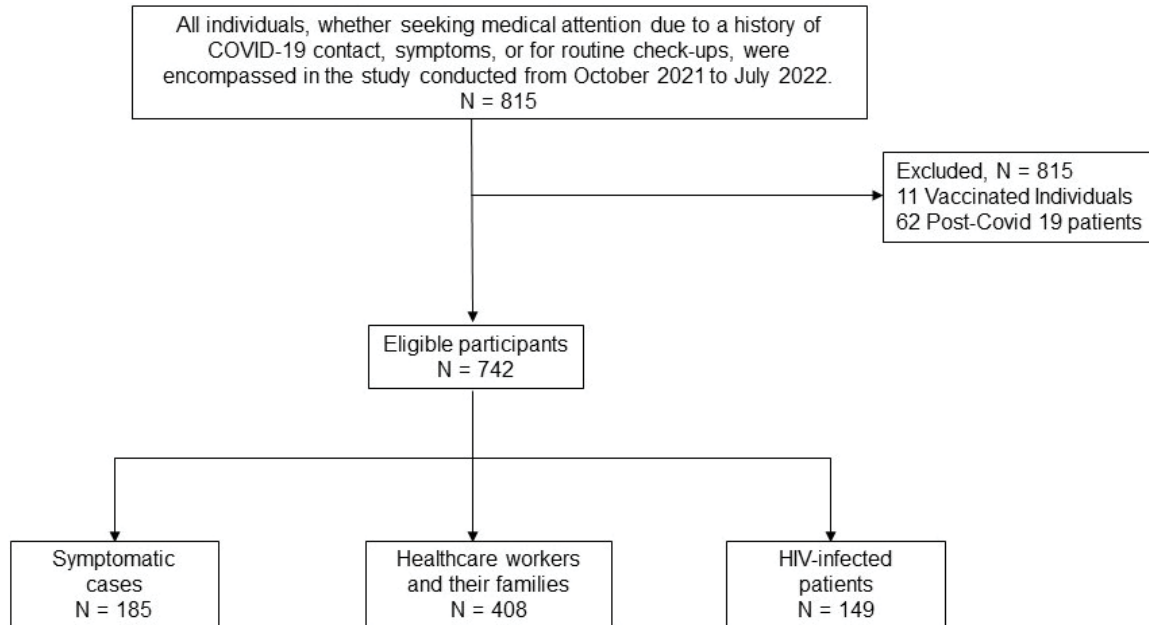

Figure 2: The group of individuals who have undergone IgG and IgM antibody tests.

Table 1: Demographic and serology testing of the participants in the study.

Sociodemographic variables	Total N = 742	Symptomatic cases N = 185	Healthcare workers and their families N = 408	HIV-infected patients N = 149
Gender, n (%)				
Female	386 (52.02)	65 (35.14)	219 (53.68)	102 (68.46)
Age				
Mean (SD)	41.37 (14.62)	43.33 (15.07)	40.15 (14.91)	42.30 (12.92)
Median (IQR)	39.00 (18.00)	40.00 (22.00)	37.00 (16.00)	42.00 (15.00)
Q1, Q3	32.00, 50.00	32.00, 54.00	32.00, 48.00	35.00, 50.00
Min, Max	3.00, 92.00	5.00, 92.00	5.00, 87.00	3.00, 81.00
CD4				
Mean (SD)				383.01 (272.47)
Median (IQR)				363.00 (416.00)
Q1, Q3				154.00, 570.00
Min, Max				3.00, 1128.00
IgM level				
Mean (SD)	1.34 (1.81)	1.76 (2.15)	1.24 (1.80)	1.10 (1.22)
Median (IQR)	0.70 (1.50)	1.00 (1.60)	0.60 (1.20)	0.60 (1.30)
Q1, Q3	0.20, 1.70	0.40, 2.00	0.20, 1.40	0.30, 1.60

Min, Max	0.00, 11.30	0.00, 10.50	0.00, 11.30	0.00, 6.40
IgG level				
Mean (SD)	22.22 (28.36)	37.13 (31.53)	15.96 (24.51)	20.83 (27.37)
Median (IQR)	0.60 (46.50)	50.40 (63.60)	0.00 (32.55)	3.50 (37.40)
Q1, Q3	0.00, 46.50	0.00, 63.60	0.00, 32.55	0.00, 37.40
Min, Max	0.00, 129.40	0.00, 116.20	0.00, 120.10	0.00, 129.40
IgM detected, n (%)	313 (42.18)	100 (54.05)	153 (37.50)	60 (40.27)
IgG detected, n (%)	369 (49.73)	129 (69.73)	164 (40.20)	76 (51.01)
Antibody Detection in the Population				
IgM-IgG-	256 (34.50)	39 (21.08)	167 (40.93)	50 (33.56)
IgM-IgG+	173 (23.32)	46 (24.86)	88 (21.57)	39 (26.17)
IgM+IgG-	117 (15.77)	17 (9.19)	77 (18.87)	23 (15.44)
IgM+IgG+	196 (26.42)	83 (44.86)	76 (18.63)	37 (24.83)

Table 2: Demographic and serology testing of individuals Living with HIV and hospitalized patients.

Sociodemographic variables	Total N = 315	Hospitalized patients N = 166	HIV-infected patients N = 149	p-value
Gender, n (%)				
Female	155 (49.21%)	53 (31.93)	102 (68.46)	<0.001
Age				
Mean (SD)	43.17 (14.25)	43.95 (15.34)	42.30 (12.92)	0.3
Median (IQR)	42.00 (18.00)	40.50 (21.75)	42.00 (15.00)	
Q1, Q3	33.00, 51.00	32.25, 54.00	35.00, 50.00	
Min, Max	3.00, 92.00	5.00, 92.00	3.00, 81.00	
IgM level				
Mean (SD)	1.44 (1.84)	1.76 (2.21)	1.10 (1.22)	0.02
Median (IQR)	0.80 (1.50)	1.00 (1.70)	0.60 (1.30)	
Q1, Q3	0.30, 1.80	0.30, 2.00	0.30, 1.60	
Min, Max	0.00, 10.50	0.00, 10.50	0.00, 6.40	
IgG level				
Mean (SD)	30.88 (30.99)	39.90 (31.35)	20.83 (27.37)	<0.001
Median (IQR)	25.40 (59.15)	53.95 (63.90)	3.50 (37.40)	
Q1, Q3	0.00, 59.15	0.00, 63.90	0.00, 37.40	
Min, Max	0.00, 129.40	0.00, 116.20	0.00, 129.40	
IgM detected, n (%)	145 (46.03)	85 (51.20)	60 (40.27)	0.07
IgG detected, n (%)	199 (63.17%)	123 (74.10)	76 (51.01)	<0.001
Antibody Detection in the Population				<0.001
IgM-IgG-	85 (26.98)	50 (33.56)	50 (33.56)	
IgM-IgG+	85 (26.98)	39 (26.17)	39 (26.17)	
IgM+IgG-	31 (9.84)	23 (15.44)	23 (15.44)	
IgM+IgG+	114 (36.19)	37 (24.83)	37 (24.83)	

with fewer females among hospitalized patients (31.93% vs. 68.46%, p-value <0.001). The age distribution was relatively similar between the groups, showing no statistically significant difference (p-value = 0.30).

IgM antibody detection did not exhibit a significant difference between the groups, with 51.20% IgM detection in inpatients and 40.27% in individuals living with HIV (p-value = 0.07). Conversely, the presence of IgG antibodies displayed a significant contrast, with 74.10% IgG detection in inpatients compared to 51.01% in people living with HIV (p-value <0.001) (Table 2). Notable disparities were noted in the combinations of IgM and IgG antibody responses between the groups, as indicated by the significant p-value (<0.001). The majority of individuals who tested positive via PCR also exhibited positive IgG results.

The clinical care algorithm, in line with Boditech guidelines, provides a detailed and systematic approach to patient management, ensuring comprehensive and effective

care. A distinction was observed between the two populations regarding the correlation between IgM and IgG levels, with Spearman correlations of 0.41 and 0.25 for hospitalized patients and people living with HIV, respectively. This indicates a stronger correlation between IgM and IgG levels in hospitalized patients compared to those living with HIV.

Discussion

Main Findings, Interpretation, and Comparison with Other Studies

In our study, we conducted serologic tests to estimate the prevalence of SARS-CoV-2 infection in at-risk individuals, utilizing these tests to identify both active and past infections. Our indicate that 42.18% of the valid samples tested positive for IgM, and 49.73% tested positive for IgG. It is noteworthy that the majority of previous studies have emphasized the suitability of serological antibody tests primarily for surveillance and prevention, with limited relevance for hospitalized patients [7-9].

Among the participants, 22.37% were emergency care patients. In this context, serology testing plays a critical role in the management of hospitalized patients, providing valuable insights into infections, immune responses, and disease progression. This perspective is particularly relevant when serology tests are employed without a well-defined care guideline and algorithm. Conversely, some authors argue that serological antibody tests can be considered for diagnostic purposes, especially for hospitalized patients, when used in conjunction with rapid diagnostic tests (RDTs) targeting IgM/IgG or RT-PCR [10-13].

Our findings align with these views, demonstrating the importance of integrating serological testing into clinical practice for a comprehensive understanding of COVID-19 infection dynamics. The seroprevalence rates observed in our study reveal the significant presence of both recent and past infections among at-risk populations. These insights underscore the need for continued surveillance and strategic use of serological testing to inform public health interventions and optimize patient care.

Healthcare Workers

Healthcare workers and their families comprised a significant portion of our study population (55%). Performing PCR tests for this group was often challenging and sometimes impossible due to cost constraints. To prevent and monitor infections, we opted to use immuno-serological tests [14-16]. The high costs of PCR tests rendered them impractical for extensive use, necessitating alternative strategies. Consequently, we implemented rigorous monitoring of healthcare personnel and their families using optimized serological tests in combination with clinical assessments (symptoms), imaging (CT scans), and biochemical markers (D-dimers). Notably, our hospital recorded no fatalities among healthcare workers due to COVID-19, which we attribute to a stringent control program [17,18].

Families of healthcare workers were also included in the monitoring efforts, as they constitute a potential infection risk for healthcare personnel during epidemics. Healthcare workers were among the highly exposed groups during the COVID-19 pandemic. However, in many instances, their family members were neither tested nor monitored simultaneously with the healthcare workers [17,19,20]. This oversight highlights the need for comprehensive infection control strategies that include the families of healthcare workers to mitigate the risk of transmission and ensure the safety of all individuals involved.

People Living with HIV

In Gabon, rigorous lockdown measures were implemented, affecting individuals living with HIV, as well as those who had experienced acute or recent infections, past infections, and acute reinfections. Interestingly, our study revealed that people living with HIV were less susceptible to reinfection compared to hospitalized individuals. Additionally, vitamin therapy was recommended for this patient cohort.

In this study, a significant number of people living with HIV had a CD4 count greater than 300, with a range from 3 to 1128. Severe immunosuppression is the primary reason for vulnerability among people living with HIV, which may explain why these individuals did not develop severe forms of COVID-19 [21].

Notably, the immune response among people living with HIV (PLWHIV) displayed significant distinctions compared to other patients (p<0.001). Despite their vulnerability, this group exhibited a remarkable ability to resist COVID-19 infections [22]. For many individual samples, no antibodies were detected. This absence of antibodies could indicate that those individuals had not been exposed to SARS-CoV-2, or it could suggest a slow immune response or lower sensitivity of the point-of-care tests. Some authors have shown that a lack of detectable antibodies is associated with reinfection [18,23].

The effectiveness of diagnosing COVID-19 depends on various factors, including the type of samples used and the stage of the disease. A highly recommended approach involves employing a multifaceted strategy that incorporates patient demographics, medical histories, clinical symptoms, and the results of both molecular and serological diagnostic tests, along with imaging data, to ensure an accurate diagnosis for individuals with COVID-19 [24]. In numerous hospitals located in economically constrained countries, the expense associated with PCR tests remains prohibitively high. Consequently, there is an urgent need to implement cost-

effective diagnostic solutions. While clinical symptoms retain their significance, the consensus among most authors is that the integration of serological diagnostics is indispensable, particularly for resource-limited nations [25-26].

Strengths and Limitations

This study has several limitations. The primary limitation is the potential selection bias, as participants may have included individuals who are more likely to go out and thus have a higher risk of exposure to the virus, as well as those who were already concerned about potential infection. Additionally, the presence of comorbidities and symptoms compatible with COVID-19 were not recorded, which could influence the interpretation of the serological data. Moreover, the cross-sectional study design does not allow for the assessment of SARS-CoV-2 antibody prevalence over time.

Despite these limitations, serological testing remains an invaluable tool in epidemiology. It can detect recent and past infections, including asymptomatic and recovered cases, providing a more comprehensive understanding of disease prevalence within a population. This capability enhances the accuracy of public health data and informs more effective intervention strategies.

Conclusion

Serology tests are essential in the ongoing fight against COVID-19, providing valuable data on immunity, vaccine efficacy, asymptomatic infections, public health strategies, and variant detection. The scientific literature strongly supports the widespread implementation of serology testing as a key component of pandemic management and recovery.

By incorporating serology testing into public health initiatives, we can enhance our understanding of the disease, optimize vaccination programs, and develop more effective strategies for controlling the spread of the virus.

References

1. Wu F, Zhao S, Yu B, et al. A new coronavirus associated with human respiratory disease in China. Nature 579 (2020): 265-269.

2. Céron DS, DAVIDO B, TUBIANA R, et al. Les formes prolongées de la COVID-19 ou COVID long : formes cliniques et prise en charge. M decine et Maladies Infectieuses Formation 1 (2022): 24-33.

3. Müller L, Ostermann PN, Walker A, et al. Sensitivity of anti-SARS-CoV-2 serological assays in a high-prevalence setting. Eur J Clin Microbiol Infect Dis 40 (2021): 1063-1071.

4. Diop BZ, Ngom M, Biyong CP, et al. The relatively young and rural population may limit the spread and severity of COVID-19 in Africa: a modelling study. BMJ Glob Health 5 (2020): e002699.

5. Njenga MK, Dawa J, Nanyingi M, et al. Why is There Low Morbidity and Mortality of COVID-19 in Africa?. The American Journal of Tropical Medicine and Hygiene 103 (2020): 564-569.

6. Hirabidian M, Bocket L, Demaret J, et al. Evaluation of a rapid semiquantitative lateral flow assay for the prediction of serum neutralizing activity against SARS-CoV-2 variants. Journal of Clinical Virology 155 (2022): 105268.

7. Cassaniti I, Novazzi F, Giardina F, et al. Performance of VivaDiag COVID-19 IgM/IgG Rapid Test is inadequate for diagnosis of COVID-19 in acute patients referring to emergency room department. Journal of Medical Virology 92 (2020): 1724-1727.

8. West R, Kobokovich A, Connell N, et al. COVID-19 Antibody Tests: A Valuable Public Health Tool with Limited Relevance to Individuals. Trends in Microbiology 29 (2021): 214-223.

9. Wang P. Combination of serological total antibody and RT-PCR test for detection of SARS-COV-2 infections. Journal of Virological Methods 283 (2020): 113919.

10. Veyrenche N, Bolloré K, Pisoni A, et al. Diagnosis value of SARS-CoV-2 antigen/antibody combined testing using rapid diagnostic tests at hospital admission. Journal of Medical Virology 93 (20201): 3069-3076.

11. Xie J, Ding C, Li J, et al. Characteristics of patients with coronavirus disease (COVID-19) confirmed using an IgM-IgG antibody test. Journal of Medical Virology 92 (2020): 2004-2010.

12. Brockwell J, Bottomley PJ. Recent advances in inoculant technology and prospects for the future. Soil Biology and Biochemistry 27 (1995): 683-697.

13. Rostamzadeh D, Mortezagholi S, Alinejad M, et al. Serological assay for anti-SARS-CoV-2 antibodies improves sensitivity of diagnosis of COVID-19 patients. Med Microbiol Immunol 210 (2021): 283-289.

14. d'Ettorre G, Pellicani V, Muratore M, et al. Occupational health surveillance of healthcare workers during COVID 19 pandemic: a narrative review: Occupational health surveillance during COVID-19 pandemic. Acta Biomedica Atenei Parmensis 93 (2022): e2022007.

15. Wiggen TD, Bohn B, Ulrich AK, et al. SARS-CoV-2 seroprevalence among healthcare workers. PLoS ONE 17 (2022): e0266410.

16. Rusakaniko S, Sibanda EN, Mduluza T, et al. SARS-

CoV-2 Serological testing in frontline health workers in Zimbabwe. PLoS Negl Trop Dis 15 (2021): e0009254.

17. Rabow MW, Huang CHS, White-Hammond GE, et al. Witnesses and Victims Both: Healthcare Workers and Grief in the Time of COVID-19 », Journal of Pain and Symptom Management 62 (2021): 647-656.

18. Jalali Nadoushan M, Ahmadi S, Jalali Nadoushan P. Serology Testing for SARS-CoV-2: Benefits and Challenges. Iran J Pathol 15 (2020): 154-155.

19. Helou M, El Osta N, Husni R. Impact of the COVID-19 pandemic on healthcare workers' families. WJCC 10 (2022): 9964-9966.

20. Folschweiller N, Teixeira J, Joshi S, et al. Immunogenicity and safety of the AS04-HPV-16/18 and HPV-6/11/16/18 human papillomavirus vaccines in asymptomatic young women living with HIV aged 15–25 years: A phase IV randomized comparative study . EClinicalMedicine 23 (2020): 100353.

21. Posada-Vergara MP, Alzate-Ángel JC, Martínez-Buitrago E, COVID-19 and HIV. Colomb Med 51 (2020): e4327.

22. Toledo-Ibarra GA, Covantes-Rosales CE, Girón-Pérez DA, et al. Niveles de IgG anti-SARSCoV- 2 en población infantil de Nayarit, México, como biomarcador de inmunidad comunitaria. Estudio de caso a 17 meses de la pandemia por Covid-19. Salud Publica Mex 63 (2021): 822.

23. Hønge BL, Hindhede L, Kaspersen KA, et al. Long-term detection of SARS-CoV-2 antibodies after infection and risk of re-infection. International Journal of Infectious Diseases 116 (2022): 289-292.

24. Saboyá-Díaz MI, Castellanos LG, Morice A, et al. Lessons learned from the implementation of integrated serosurveillance of communicable diseases in the Americas. Revista Panamericana de Salud Pública 47 (2023): e53.

25. Sidiq Z, Hanif M, Dwivedi KK, et al. Benefits and limitations of serological assays in COVID-19 infection. Indian Journal of Tuberculosis 67 (2020): S163-S166.

26. Dramé M, Teguo MT, Proye E, et al. Should RT-PCR be considered a gold standard in the diagnosis of COVID-19?. Journal of Medical Virology 92 (2020): 2312-2313.