False-Positive Human Immunodeficiency Virus Reactivity in COVID Patients: A Word of Caution

Sir,

Human immunodeficiency virus (HIV) testing as a part of screening is accomplished by TRI-DOT Rapid HIV flow-through test (DIAGNOSTIC ENTERPRISES, H.P, India) and VIDAS® HIV DUO ULTRA, 4th generation assay (BioMérieux, Marcy-l'Etoile, France) at the Serology Laboratory of our center. We report two patients from the intensive care unit admitted at our dedicated COVID center who falsely reacted to HIV-1/2 by the VIDAS® HIV panel.

In the first case, a 69-year-old male was admitted with COVID-19 associated respiratory distress on April 16, 2021. The patient developed COVID ARDS, sepsis, and acute kidney injury. He succumbed to cardiac arrest on day 23. Viral markers for HIV, HBsAg, and HCV were requested on day 14.

We noted that TRI-DOT was nonreactive, whereas VIDAS was reactive with 2.48 s/CO ratio for anti-HIV ½, antigen (p24) was not detected by VIDAS (A signal/cutoff ratio of ≥0.25 is considered reactive). He tested nonreactive for HBsAg (VIDAS®) and HCV (HCV TRI-DOT). COVID antibodies using VIDAS® severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) IgG and IgM were found 0.87 (s/CO) for IgM and 15.50 for IgG. (s/CO values of ≥1 are considered reactive).

A repeat sample on day 17 gave similar results. (TRI-DOT being nonreactive and VIDAS being reactive with 2.91 s/CO ratio for anti-HIV ½). Part of the sample was tested on Abbott Architect platform (Abbott Laboratories, Abbott Park, Illinois, USA) and found reactive with 1.2 s/CO ratio (s/CO values of ≥1 are considered reactive).

The second case was a 9-year-old boy admitted on May 7, 2021, with seizure, and dehydration and diagnosed with COVID by reverse transcription-polymerase chain reaction. Viral markers for HIV, HBsAg, and HCV were requested on day 12 of admission.

We found TRI-DOT nonreactive and VIDAS reactive with 1.22 s/CO ratio for anti-HIV ½. However, antigen (p24) was again not detected. He tested nonreactive for HBsAg (VIDAS®) and HCV (HCV TRI-DOT).

With repeat sample on day 14, TRI-DOT gave a nonreactive result, and VIDAS® HIV was reactive with a s/CO ratio of 0.89. Part of the sample tested on Abbott Architect platform was found nonreactive. COVID antibodies detected by VIDAS® SARS COV-2 IgG and IgM were 0.27 (s/CO) for IgM and 7.20 for IgG.

The clinical and laboratory parameters of both patients are given in Table 1.

Conclusively, low titers of antibodies are expected in recent HIV infection, very advanced disease, and presence of broadly cross-reacting antibodies. Advanced disease was ruled out on the basis of presenting illnesses, whereas in early HIV infection, the presence of antigen is expected. This leaves us with the cross-reacting antibodies. False-positive reactions with other 4th generation assays have been seen with schistosomiasis, Epstein–Barr virus, and malignancy.[1-3] During the current pandemic, Tan *et al.* also reported two COVID patients who had falsely tested reactive to HIV, on Abbott Architect, whereas VIDAS® HIV and MP Biomedicals HIV immunoblot were negative.[4] The coronavirus spike proteins and envelope glycoproteins of HIV are structurally homologous, extensively glycosylated class 1 type fusion proteins,[5] and some incidents of cross reactivity are expected with an ongoing pandemic.

Acknowledgment

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

Table 1: Clinical and laboratory work up of both the cases

Parameter	Case 1		Case 2	
Age (years)	69		9	
Gender	Male		Male	
Clinical findings on admission	Fever, cough and breathlessness		Hypernatremia dehydration with seizures	
Provisional diagnosis	COVID pneumonia		Suspected seizure disorder with COVID	
Duration of stay	23 days		20 days	
Laboratory parameters	Day 1	Day 14	Day 1	Day 12
CBC				
TLC	6400	6200	9000	11100
DLC	$N_{87}L_{9}M_{4}E_{0}$	$N_{83}L_{11}M_{4}E_{2}$	$N_{82}L_{13}M_{4}E_{1}$	$N_{86}L_{8}M_{5}E_{1}$
Platelets ($\times 10^5$)	1.19	0.34	1.82	1.75
KFT				
Urea (mg %)	94	87	27	173
Creatinine (mg/dL)	1.4	1.1	0.6	3.1
LFT				
AST (U/L)	40	30	27	30
ALT (U/L)	23	31	50	27
Bil (I) (mg/dL)	0.5	0.8	0.8	0.8
Bil (D) (mg/dL)	0.3	0.3	0.2	0.2
ALP (U/L)	34	37	268	175
Inflammatory markers				
IL6 (pg/mL)	88.20	>1620.20	4.26	75.37
Ferritin (ng/mL)	>1500	891.7	92.5	41.6
Procalcitonin (ng/mL)	0.48	1.51	--	25.36
X-ray chest	Ground glass opacities		Ground glass opacities	
Treatment	Symptomatic management for fever and cough, levothyroxine, inotrope- adrenaline, amiodarone for atrial fibrillation, antibiotics- meropenem, tigecycline and anidulafungin; Respiratory distress gradually worsened, intubation and mechanical ventilation was started		IV fluids, levetiracetam, inotrope (adrenaline, weaned off in 2 days), IVIG, methylprednisolone 2 mg/kg/day- tapered to 1 mg/kg/day, antibiotics- meropenem, tigecycline and fluconazole; was intubated briefly, hemodialysis done on 20th May because of deranged kidney function tests	
Outcome	Expired on day 23		Discharged on day 20	

CBC:Complete blood counts, TLC: Total leukocyte count, DLC: Differential leukocyte count, NLME: Neutrophils, Lymphocyte, Monocyte, Eosinophils, KFT: Kidney function test, LFT: Liver function test, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatise, IL6: Interleukin 6, IV: Intravenous, IVIG: Inravenous Immunoglobulins

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