

HUMAN IMMUNODEFICIENCY VIRUS (HIV): A DIAGNOSTIC DILEMMA

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ABSTRACT

Human immunodeficiency virus is a blood borne virus and is being routinely screened in the blood banks since 1983. The sensitivity and specificity of HIV tests have improved dramatically over the years, but even then, false positive results do occur, which need confirmatory testing. A young male who arrived at Armed Forces Institute of Transfusion (AFIT), Rawalpindi, for blood donation, was repeatedly “positive” on serological assays. Nucleic acid amplification test (NAT) was performed which gave a “Negative” result. Line immunoassay (LIA) was performed to solve the discrepancy in test results.

Keywords: False positive, Human immunodeficiency virus, Laboratory Diagnosis.

How to Cite This Article: Rathore A M, Niazi K S, Rathore A M, Yazdani S M. Human Immunodeficiency Virus (HIV): A Diagnostic Dilemma. *Pak Armed Forces Med J* 2022; 72(Suppl-2): S397-398.

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INTRODUCTION

Human immunodeficiency virus (HIV) is an emerging viral disease in Pakistan. It is currently concentrated in high risk groups, with the possibility of spill over in the general population.¹ Over the years, laboratory tests for diagnosis of HIV have improved both in sensitivity and specificity along with automation, thereby reducing laboratory errors. The latest serological tests, both the enzyme linked immunosorbent assays (ELISA) and chemiluminescence microparticle immunoassays (CMIA), have incorporated antigen p24 to anti HIV 1/2 (combo or fourth generation assays) thus making these tests very sensitive along with reduction in window period of detection.² Instead of all these advancements, problems do arise when false positive HIV results are generated, usually due to cross reacting antibodies.³ Therefore, confirmatory tests like nucleic acid testing or Western Blot/Line immunoassays (LIA) must be done to rule out the possibility of false positive results.⁴

CASE REPORT

A 31 years old male visited Armed Forces Institute of Transfusion (AFIT), Rawalpindi, for blood donation on 11th March, 2018. His blood was screened for transfusion transmissible infections (TTIs) on an automated CMIA analyzer, Abbott Architect iSR2000. He was negative for antibodies to hepatitis C virus, anti-treponemapallidum antibodies and hepatitis B

surface antigen. However, the individual was found “positive” on serology for (HIV). The serological result for anti HIV1/2 ± p24 assay (Combo assay) had a signal to cutoff ratio (S00/Co) value of 71 (Positive S/CO >1). For confirmation, NAT was performed on Taqman screen MPX 2.0 s201 Cobas (Roche diagnostics). The NAT result was “negative”. The blood donor was recalled repeatedly but due to certain domestic issues, he reported after a month from initial screening. Detailed history of exposure for HIV was taken but no specific risk factor could be identified. Repeat testing was done both by serology and NAT. In serology, the S/Co value dropped to 44 (from 71 previously) but was still positive. NAT done on the re-visit sample, by transcription mediated amplification (TMA) method, one of the techniques to detect nucleic acid, performed on Panther (Grifols), was “negative”. The blood donor was again recalled second time after a month and retested for HIV, both by serology and NAT. Serology result for HIV was 25 (showed S/CO of lower than the previous two results) but still higher than the cut off value as per manufacturers instruction (Positive S/CO >1). However, nucleic acid testing results by both Grifols and Roche were negative. The sample was sent to Armed Forces Institute of Pathology (AFIP) for reconfirmation. In AFIP, tests were repeated on Abbott architect by CMIA, 4th generation ELISA (BioRad) and by LIA, Geenius HIV 1/2 Confirmatory Assay (BioRad) (Table-I). The result of CMIA (Abbott Architect) was “positive”, whereas ELISA was “negative” and LIA was “negative” for HIV1 and “Indeterminate” for HIV 2 (Figure-1).

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Received: 22 Nov 2018; revision received: 10 Feb 2020; accepted: 18 Feb 2020

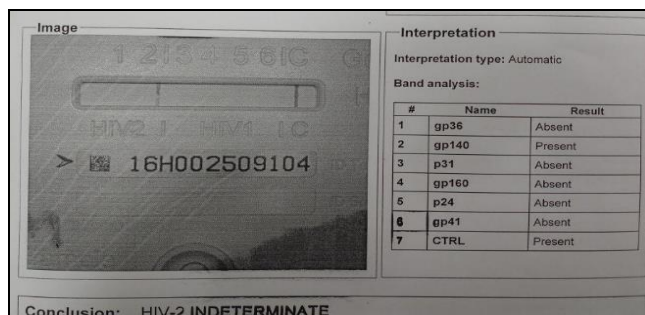


Figure: Negative for HIV 1 and Indeterminate for HIV 2 on Line immunoassay (LIA).

Table: The tests performed and their results.

Place	Method	1st Visit	2nd Visit	3rd Visit
AFIT	CMIA	Positive	Positive	Positive
	NAT (PCR/TMA)	Negative	Negative	Negative
AFIP	CMIA	-	-	Positive
	PCR	-	-	Negative
	ELISA	-	-	Negative
	LIA	-	-	HIV 1 Negative HIV 2 Indeterminate

DISCUSSION

There is currently a concentrated HIV epidemic in Pakistan,⁵ especially in high risk groups.⁶ Screening of blood for TTIs is important for preventing disease transmission through transfusion. In most of the blood banks, blood components are prepared from donated blood and hence one missed infection in a blood donor can lead to disease transmission in three different recipients.⁷ Nowadays, chemiluminescence based assays are preferred over ELISAs, both in diagnostic laboratories as well as blood banks, because of their improved sensitivity and ease of performing test, although at a higher price. There are many reasons for a false positive HIV test result; like cross reacting antibodies, auto antibodies, recent vaccination, liver diseases and cancers etc.⁸ Confirmation of serology positive HIV was previously done by Western blot, a technique difficult to perform with low throughput of samples and frequently indeterminate test results.⁹ Nucleic acid testing (NAT) has replaced western blot/LIA as a confirmatory test.¹⁰ However, in difficult and confusing results like the reported case, western blot/LIA do help in reaching the right diagnosis.¹¹ In this case, the individual repeatedly tested positive on CMIA. However, 4th generation ELISA was negative. NAT was repeatedly negative. In LIA performed in Armed Forces Institute of Pathology AFIP, the individual was negative for HIV-1 and indeterminate for HIV-2. As HIV-2 is not

present in this geographic region,¹² and the constantly decreasing trend in the antibodies levels observed over the two months period also suggest that the indeterminate result for HIV-2 on LIA can be disregarded and this donor, in fact, had a false positive test result. This case highlights the dilemma in diagnosis of HIV with highly sensitive assays. Many diagnostic laboratories and blood banks use chemiluminescence assay routinely and such cases as we have reported here, may be declared as “initially reactive” for HIV 1/2. Since confirmatory assays are not frequently available or may not be performed due to the added cost, many patients or blood donors might take a while before being declared HIV negative by confirmatory tests.

CONCLUSION

False positive results for HIV can occur after using good testing platforms including automated chemiluminescence based assays with even higher S/Co values. These results must be confirmed by either PCR or western blot/LIA. The interpretation of HIV positive cases on serology sensitive assays, even with high S/Co values must be done with caution.

Conflict of Interest: None.

Author’s Contribution:

MAR:, SKN:, MAR: Conception, analysis interpretation, MSY: Analysis, Interpretation of data.

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