Original article:

Diagnosis of syphilis in HIV+ve and HIV –ve patients

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Abstract:

Introduction: A new dimension has been added to the control of sexually transmitted diseases in India because of the emerging epidemic of acquired immunodeficiency syndrome. Serology remains the mainstay of laboratory diagnosis of syphilis; which is prevalent among all STDs in India. So, we have tried to set up the testing algorithm for syphilis in HIV positive and HIV negative patients.

Material and methods: 100 samples from HIV positive and negative patients were tested using VDRL, RPR and TPHA tests.

Result: Out of 29 HIV positive sera 5(18.5%) were positive by VDRL, RPR and TPHA tests. Among 71 HIV negative sera, 27(38%) were positive by VDRL, RPR and TPHA while 3(4.2%) were positive by RPR-TPHA and 3(4.2%) were positive only by TPHA test.

Conclusion: We suggest RPR-TPHA as the testing algorithm for HIV positive as well as negative patients.

Key words: Treponemes, HIV, VDRL, TPHA, RPR

Introduction:

A new dimension has been added to the control of sexually transmitted diseases in India because of the emerging epidemic of acquired immunodeficiency syndrome. Syphilis is prevalent among all STDs in India. It is caused by Treponema pallidum. Serology remains the mainstay of laboratory diagnosis of syphilis; but during very early stage of infection, direct detection of treponemes in material from lesion by dark ground or fluorescent microscopy is necessary.

Serological screening of syphilis has gained an importance because of certain characteristics. Syphilis in pregnant women may lead to still birth and congenital syphilis. It also leads to perpetual sexual transmission and tertiary syphilis in long standing cases. For the serodiagnosis of this disease validated serological tests are available at relatively low cost and the patient is amenable to treatment with complete cure. (1).

The serological tests for syphilis may be difficult to interpret in immunocompromised individuals where humoral responses could be impaired. In HIV positive patients, unusual serological responses have been reported in syphilis, such as much higher VDRL titers. Delayed appearance of seroreactivity has also been reported in HIV positive patients. So, the current study was undertaken to evaluate the performance of two nontreponemal tests and one treponemal test in presence and absence of HIV infection.

Material and methods:

The study group consisted of 100 patients (male and females) randomly selected from the serum samples received in Serology section of Department of Microbiology. These samples were from patients
visiting OPD clinic and admitted at Sassoon General Hospital, Pune. Patients with past history of syphilis were excluded. Clinically suspected syphilis patients (without past history of syphilis) were included in the study. Considering patient’s HIV status, they were classified as HIV positive and HIV negative. 23 HIV positive and 71 HIV negative patients were included in the study. 23 sera were collected from healthy blood donors as control.

Result:
Total sera collected were 100.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Positive by</th>
<th>HIV positive Sera</th>
<th>HIV negative sera</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>29</td>
<td>71</td>
</tr>
<tr>
<td>1</td>
<td>VDRL, RPR &amp; TPHA</td>
<td>5 (18.5%)</td>
<td>27 (38%)</td>
</tr>
<tr>
<td>2</td>
<td>RPR &amp; TPHA</td>
<td>Nil</td>
<td>3 (4.2%)</td>
</tr>
<tr>
<td>3</td>
<td>RPR</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>4</td>
<td>TPHA</td>
<td>Nil</td>
<td>3 (4.2%)</td>
</tr>
<tr>
<td>5</td>
<td>VDRL</td>
<td>Nil</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>5 (18.5%)</td>
<td>34</td>
</tr>
</tbody>
</table>

Table 1: Test results by RPR, VDRL and TPHA of HIV positive and negative sera.

Two sera from the control group showed positive VDRL test at low titers (1:4).

Discussion:
Simultaneous infection with *Treponema pallidum* and HIV can become a serious health problem. HIV changes the natural course of syphilis and also response to therapy. Syphilis being a disease with broad range of manifestations, evaluation of laboratory and clinical findings of syphilis-HIV co-infected patients is intricate. Due to atypical serological response to treponemal antigen in HIV positive patients, interpretation of serological tests for syphilis may become difficult.

Incidence of syphilis in the present study was as follows-18.5% in the HIV positive group (5/29) and 38% in HIV negative group (27/71). Total incidence being 32%. Quinn TC et al (4) and Ansell DA et al (5) noted a higher incidence of syphilis in HIV positive patients (close to 30%) while Schofer H et al (6) and Malone et al (7) showed the incidence to be 4-6%.

We observed high incidence of syphilis (38%) in the HIV negative group. This we feel is a matter of concern. It has been noted on the basis of the collaborative study on risk factors for HIV that STDs including syphilis are associated with an increased risk for HIV infection among both homosexual and heterosexual persons (2). Probably promiscuous sexual behavior that increases the risk of acquiring STDs, also increase the risk of HIV transmission. Furthermore, ulceration and inflammation caused by STDs are implicated as the cofactors for acquiring HIV infection. Recent data suggest that in presence...
of other STDs, individuals are 3 to 5 times more likely to acquire HIV if exposed to the virus through sexual contact. (3) Considering the close association of syphilis and HIV, we also suggest that all patients with newly diagnosed syphilis should be counseled for repeated HIV testing after a fixed interval.

The VDRL test in the present study showed a false positive percentage of 1% of the total population. This 1% false positivity with VDRL was seen in HIV negative group and not in HIV positive group in the present study. Wiwanitkit Viroj (8) documented significantly lower rate of biological false reactive VDRL (1.3%) among HIV infected patients, while Ganapathysundaram et al (9) reported the rate of biological false reactive VDRL among prostitutes of India to be 10.6%.

RPR test did not show any false positivity in either of the groups. Joyanes et al documented an incidence of biological false positives of RPR to be 15% in HIV positive and 1.2% in HIV negative group.(10) Similar results were also obtained by Rompallo et al (11) indicating incidence of biological false positives is much higher in HIV positive group. Our results contradict with the above said documented results and nontreponemal tests were found to be specific in both HIV positive and negative group. In the general population (HIV negative group), the biological false positive VDRL and RPR test generally returns to negative within 14 weeks, without other clinical significance. (8) However, in the present study, it was not possible to follow up the biological false positive test to ascertain the clinical course. Further prospective study in the HIV positive and negative patients with biological false positive results to assess the seroconversion pattern is recommended.

The sensitivity of nontreponemal and treponemal tests for syphilis increases with duration of infection and ranges from approx. 75% in primary stage to virtually 100% in the secondary stage (12). In general, the sensitivity of treponemal tests continues to approximate 100% in late syphilis in contrast to nontreponemal tests which are more practical and cost effective for initial screening but have diminished sensitivity in late syphilis. Therefore, in HIV negative patients, it will be useful to consider both a nontreponemal and treponemal test as the diagnostic strategy. In the present study, among the nontreponemal tests, RPR was found to be more specific and sensitive than VDRL. Both these tests use cardiolipin, lecithin and cholesterol containing antigen to measure antilipoidal antibodies. Better performance of RPR remains unexplained and needs to be confirmed on large no. of samples. So, in HIV negative group, RPR followed by TPHA should be the testing algorithm.

A negative RPR or VDRL test may not rule out syphilis in patients with HIV infection (13). Although, the sensitivity of these serological tests in diagnosing secondary syphilis is generally very high, rare case reports have described seronegative secondary syphilis in patients with HIV infection (13) suggesting that some patients may fail to develop normal antibody responses to T. pallidum.

In addition, a negative treponemal test may not rule out syphilis. In a study of patients with RPR test reactive at a dilution greater than 1:8, antibodies to T. pallidum membrane antigens were detected in a few patients with persistently negative FTA-Abs test results (14). This finding raises the possibility that some reactions that appear to be biological false positive may in fact represent syphilis with negative treponemal serological tests. This study raises
question regarding sensitivity and specificity of the treponemal tests in diagnosing syphilis in HIV infected patients. To confirm the above data, extensive study needs to be undertaken but till then we should consider the sensitivity and specificity of the treponemal test to be high in the HIV infected patients beyond the primary stage of infection. Considering the results obtained in the present study in HIV infected patients and varied immunological response documented in different studies, we suggest the combination of RPR and TPHA as the testing algorithm for the diagnosis of syphilis in HIV infected patients.

**Conclusion:**
We recommend RPR followed by TPTA as the testing algorithm for the diagnosis of syphilis in HIV positive and negative patients.

**References:**