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A preliminary study to characterize patients diagnosed with syphilis attending a tertiary care centre in South India

SUSMITHA KARUNASREE P JAMESGNANAKAN
Department of Microbiology,
CHRISTIAN MEDICAL COLLEGE

Abstract :
Syphilis is a common sexually transmitted infection caused by Treponema pallidum. The infection passes through distinct primary, secondary, latent and tertiary stages and these stages have implications in diagnosis and treatment. Serological tests are the mainstay in diagnosis and follow up of syphilis. The study was conducted to determine the current scenario of syphilis in a 2400 bedded tertiary care centre in south India. Ninety seven syphilis patients confirmed by the Treponema pallidum hemagglutination test (TPHA) were identified from the laboratory records from the years 2011 to 2013. Electronic medical records of the patients were sought to gather information on clinical details and coexisting sexually transmitted infections.Males were predominant in number. From the patient records available, latent stage was found to be a more common stage at presentation to the hospital followed by neurosyphilis. There was one case of fetal death in a syphilis patient brought with eclampsia to the labor room and one case of congenital syphilis which was lost to follow up. Other virus borne sexually transmitted infections like HIV, Hepatitis B and C were seen in 16 patients from details available on 78 patients. HIV was the commonest among the three. Syphilis is still prevalent and individuals at risk need to be identified and screened. Antenatal screening and appropriate therapy has reduced fetal loss to a large extent in pregnancy. Other agents of bacterial and viral etiology should also be screened for when the patient is diagnosed with syphilis or any sexually transmitted infection.

Keyword:
Syphilis, TPHA, VDRL, Sexually transmitted infections

INTRODUCTION:

Syphilis is a common infectious disease worldwide caused by the spirochete *Treponema pallidum* .It can be acquired by sexual contact, passage through the placenta (congenital syphilis),

close contact with an active lesion, primarily a chancre or condyloma, transfusion of contaminated fresh human blood, or accidental direct inoculation. Congenital syphilis occurs most frequently when the fetus becomes infected in utero. Accidental direct inoculation can occur by needle stick or during handling of infected clinical material. Syphilis, remains a global health problem, with more than 12 million cases occurring yearly worldwide, especially in underdeveloped countries (1). Within hours to days after T. pallidum penetrates the intact mucous membrane or gains access through abraded skin, it enters the lymphatics and bloodstream and disseminates throughout the body. The disease progresses through distinct primary, secondary, latent and tertiary stages. Primary syphilis is the stage of initial inoculation of T pallidum; in secondary syphilis there is a bacteremia and wide dissemination of T.pallidum; and late (tertiary) syphilis relates to the chronic, end organ complications (particularly cardiovascular and neurological) of syphilisoften many years after initial infection. The ulcers that appear in primary and secondary syphilis are rich in treponemes; venereal transmission occurs through direct contact with these lesions. The stage of the disease at which the patient presents has implications for diagnosis and treatment. Although *T. pallidum cannot be grown in culture, there are many tests for the direct and indirect diagnosis of syphilis. Direct diagnostic methods include the detection of T pallidum by microscopic examination of fluid or smears from lesions, histological examination of tissues or nucleic acid amplification methods such as polymerase chain reaction (PCR).*Indirect diagnosis is based on serological tests for the detection of antibodies. Serological tests fall into two categories: non-treponemal tests for screening, and treponemal tests for confirmation. All non-treponemal tests measure both immunoglobulin (Ig) G and IgM antiphospholipid antibodies formed by the host in response to lipoidal material released by damaged host cells early in infection and lipid from the cell surfaces of the treponeme itself. All treponemal tests use *T* pallidum or its components as the antigen. Despite their shortcomings and the complexity of interpretation, serological tests are the mainstay in the diagnosis and follow-up of syphilis. Moreover, latent syphilis can only be diagnosed by serological tests.Enzyme immunosorbant assays (EIA) with almost 100% sensitivity and specificity are being used increasingly as screening tests for syphilis in the developed countries (2). However, an EIA cannot detect reinfection of syphilis. Non treponemal tests are rapid, simple and inexpensive. They are the only tests recommended to monitor the course of disease during and after treatment. Non-treponemal tests can also serve to detect reinfection. The main limitations of non-treponemal tests are their reduced sensitivity in primary syphilis and late latent syphilis, false-positive results due to cross reactivity and the potential for false-negative results due to prozone reactions.The relation between HIV and syphilis is being extensively debated and researched. Syphilis is most common among individuals who are at risk of other sexually transmitted infections, such as HIV. The serological tests, and treatment response among individuals with HIV infection who also have syphilis are usually the same as among individuals without HIV infection who acquire syphilis. Good evidence shows that ome differences in clinical presentation do exist between HIV positive and negative individuals presenting with early syphilis (3,4). Late syphilis may also develop more rapidly in HIV positive individuals, but the evidence for this is confined to

case reports (5,6). The current study was conducted to determine the current scenario on syphilis in a 2400 bedded tertiary care centre in South India.

AIM OF THE STUDY:

To characterize the patients diagnosed with syphilis attending a tertiary care centre in south India over a period of 3 years.

OBJECTIVES:

1. To identify syphilis patients from laboratory records from the year 2011 to 2013.

2 To study the patient clinical history available from the hospital's electronic medical records.

To identify other sexually transmitted diseases in these patients.

PATIENTS AND METHODS:

A retrospective study design was adopted. All syphilis cases confirmed by T.pallidum hemagglutination test (TPHA) from the year 2011 to 2013 were selected from the laboratory records. Using the hospital number of the patient, clinical information stored in the electronic clinical work station was accessed, to gather information on the diagnoses made. Where available, details about disease outcome were captured with special emphasis on neurosyphilis, congenital syphilis and fetal loss in pregnancy. Information on other sexually transmitted diseases was also obtained on those who were tested for the same.

Serological tests for syphilis:

a. VDRL

The VDRL test was performed according to the procedure followed in the Clinical Microbiology department (7). Briefly the test protocol is as given below. Antigen was procured from the Laboratories of Serologist, Calcutta and a suspension was made using buffered saline before each batch of testing. Procedure as per the manufacturer's instructions was followed. Details regarding the testing conditions like room temperature at 23ºC– 29º C, VDRL rotator set at 180rpm, heat inactivation of serum at 56ºC for 30 minutes and stipulated antigen volume (60 drops/ml for serum samples and 100 drops/ml for CSF samples) were strictly followed and recorded every day before performing the test. The antigen suspension thus made was tested on known positive (4+, 2+ and 1+) and negative control sera. To 50µl of inactivated serum, a drop of antigen suspension was added on a VDRL slide and rotated for 4 minutes at 180rpm. The tests were read immediately using a total magnification of 100X. All the weakly reactive, reactive and doubtful reactions were re-tested in dilutions and the reciprocal of the highest dilution of VDRL reactivity was taken.

b. *Treponema pallidum hemagglutination test (IMMUTREP® TPHA,OMEGA Diagnostics,Scotland, UK)*

is a treponemal test which employs T.pallidum sensitized and unsensitized formolizedtanned erythrocytes and was performed as per manufacturer's instructions. When diluted samples are mixed with sensitized erythrocytes, antibodies to the sensitizing antigencause agglutination of cells forming a characteristic pattern at the bottom of the microtitre plate well.In the absence of antibody, a compact button is formed. The manufacturer's instructions were strictly adhered to while performing the test. The test was

performed on a microtitre plate. The samples were diluted using the diluent provided with the kit to attain two 25µl rows of final dilution of 1/80. 75µl each of control and test cells were added to these two rows respectively and agglutination patterns were looked for after 30 minutes of covering and letting it stand at room temperature. Agglutinated cells formed an even layer over the bottom of the well. Non -agglutinated cells formed a compact button in the centre of the well. Weakly agglutinated cells formed a characteristic ring pattern.Frequency, mean, median and percentages were calculated using Microsoft Excel 2007 (Microsoft Office, Redmond, WA, USA).

RESULTS:

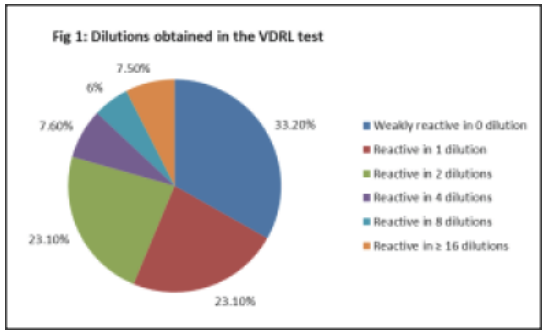
Ninety seven patients with positive TPHA were identified from the year 2011 to 2013. Of these, 57 (58.7%) were males and 40 (41.2%) were females. The mean age of patients presenting with syphilis to the hospital is 41.36 (SD 12.98). Range of the age groups was 2 months to 78years. VDRL test was positive in 65 (67%) of the 97 patients. Ninety one samples were serum samples and six of them were cerebrospinal fluid samples. The following is a table (Table 1) showing the number of patients from the different units who were diagnosed to have syphilis.

Unit	Number of patients	Percentage
Dermatology	39	40.2%
General Medicine	13	13.4%
Obstetrics & Gynecology	10	10.3%
Neurology	8	8.2%
Ophthalmology	5	5.1%
Others*	22	14%

*Reproductive Medicine Unit, Infertility clinic, Neonatology, Low cost care, outreach clinics etc

Maximum numbers of positives were from Dermatology department and the VDRL test was performed on patients with a history of high risk behavior.

Of the 65 VDRL positive patients, the percentages of patients positive in the different serum dilutions are represented in the following pie chart (Fig 1).



Of the eight samples sent from Neurology, five were non reactive and the remaining three were reactive in less than 2 dilutions in the VDRL test. Amongst the 10 samples sent from Obstetrics and Gynecology, 2 were non reactive and rest were reactive at various dilutions ranging from 0 to 256dilution. Six of the ten samples were taken from pregnant women.From the patient records, data regarding the stage of syphilis at the time of hospital visit could be retrieved for 40 patients. The stage of illness of these 40 patients is as given in Table 2.

Table 2: Stage-wise distribution of cases

Stage of syphilis	Number of patients	Percentage
Secondary syphilis stage	3	7.5%
Latent stage	28	70%
Neurosyphilis	9	22.5%
Total	40	100%

Of the six pregnant women, five of them delivered healthy term babies. There was one case of fetal death. Congenital syphilis was recorded in one child presenting to the Pediatrics department. However, the child was lost to follow up.

In 78 of the 97 syphilis cases, details of other sexually transmitted diseases (HIV, Hepatitis B and Hepatitis C) were available. Ten of them (12.8%) were HIV positive, 6 (7.6%) were Hepatitis B positive, 1 patient (1.2%) was Hepatitis C positive. One of these patients had infection with both HIV and Hepatitis B.

DISCUSSION:

Syphilis is a common infection worldwide. Serology is the main stay of diagnosing the infection. In the present study VDRL and TPHA were the serological tests performed on the patients. This is done as a preliminary study to evaluate the current trend in syphilis distribution across patients attending a tertiary care centre. Males were predominant in number. A majority of the patients presented to dermatology department and were placed under the latent syphilis category. High risk sexual behaviour, more than the presence of any skin lesions, was the commonest reason for performing VDRL test. Information on syphilis in pregnancy was carefully sought from the medical records available. There was one fetal loss. The mother did not have any antenatal visits during the entire pregnancy.She was brought with eclampsia and an emergency C section was performed on her. The primary cause of fetal loss is hence debatable. The rest of the women delivered normal term babies. This number is insignificant when compared to a previous study conducted at the same centre on fetal loss in syphilis positive pregnant mothers (8). We attribute this to strict adherence to screening protocol in the antenatal clinics and timely administration of drugs. No conclusions could be made on congenital syphilis as the one child who presented thus was lost to follow up. Neurosyphilis was the second common presentation observed in the study group.Syphilis is considered common among individuals who are at risk of other sexually transmitted infections, such as HIV and Hepatitis B (9). Information on sexually transmitted diseases of viral origin was available for 78 of the 97 patients. Dual infections with HIVor HBsAg or HCV were observed in 16 and the commonest was HIV. Screening for many of these viral infections was based on diagnosis of syphilis. Hence it should be made mandatory to look for these other STIs also in people with high risk sexual behaviour. However, information on screening for agents of bacterial etiology was not available. This could have shed more light on the dynamics of mixed bacterial STIs. This information will be useful as a preliminary audit for any future studies on syphilis in particular and STIs of bacterial & viral etiology.

LIMITATIONS:

Clinical data was not available for all the patients from the electronic database. A prospective study would enable better understanding of the disease dynamics in itself and in relation to other STIs.

CONCLUSIONS:

Syphilis is still prevalent and individuals at risk need to be identified and screened. Antenatal screening and appropriate therapy has reduced fetal loss to a large extent in pregnancy. Other agents of bacterial and viral etiology should also be screened for when the patient is diagnosed with syphilis or any sexually transmitted infection.

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