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Original Article

Microbiology Section

Syphilis Screening in Pre-procedural Patients at a Tertiary Cardiac Care Centre in India

J NAVEENA[1], KR NISHANTH[2], MP NANDINI[3], CN MANJUNATH[4]

ABSTRACT

Introduction: Routine pre-procedural screening for blood-borne infections is a common practice despite lack of standard guidelines. The incidence of syphilis has shown an upward trend in recent years.

Aim: To determine the prevalence and clinical significance of routine screening for syphilis in pre-procedural patients in tertiary care cardiac centre.

Materials and Methods: This prospective study included consecutive patients undergoing surgical and percutaneous invasive procedures at a tertiary cardiac care centre from March 2017 to August 2017. All patients were screened for syphilis using ELISA for detection of *Treponema pallidum* IgG antibodies. All patients who were positive for ELISA were confirmed with *Treponema pallidum* Haemagglutination Assay (TPHA).

Results: A total of 13,865 patients were screened and the seropositive rate was 0.45%. Most patients were in the age group of 51-70 years (71.4%) and were male (76.2%). Three patients had manifestation of cardiovascular syphilis and two patients were positive for HIV also. There was no reported incidence of needlestick injury or mucus membrane exposure to blood products during the procedures.

Conclusion: Routine pre-procedural screening for syphilis is not beneficial due to low seroprevalence. Screening must be limited to at risk individuals.

Keywords: Enzyme linked immunosorbent assay, *Treponema pallidum* hemagglutination assay, Venereal disease research laboratory

INTRODUCTION

Routine screening for blood-borne infections as a part of pre-procedural tests is a common practice in many centres. Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV) and syphilis are the most common infections screened. There are no standard recommendations for screening of blood-borne infections before invasive procedures. There have also been concerns about excessive expenditure on inappropriate tests done pre-procedurally [1,2]. Though the true prevalence of syphilis is India is not known, an increase in the prevalence of syphilis has been noted in the United Kingdom (UK), United States of America (USA), and some parts of India [3-6]. Venereal Disease Research Laboratory (VDRL) and Rapid Plasma Reagin (RPR) are still the most commonly used tests all over the world for screening of Syphilis [7]. Sensitivity of nontreponemal tests (RPR and VDRL) are estimated to be 78-86% for detecting primary syphilis, 100% for secondary syphilis and 95-98% for detecting latent syphilis. Specificity ranges from 85-99% [8]. Nontreponemal tests are based on the reaction of cardiolipin with nonspecific antibodies produced in response to syphilitic infection. The traditional algorithm for detection of syphilis consists of using a nontreponemal test which is followed by a treponemal test which remains the standard in many parts of the world [9]. In recent years, the use of Enzyme-Linked Immunosorbent Assay (ELISA) for detection of *Treponema pallidum* antibodies has shown to have higher sensitivity and specificity compared to conventional tests which had lead to increased use of reverse algorithm for syphilis detection [9]. Transmission of syphilis through blood products and occupational exposure has been reported [10,11].

In this study, we sought to examine the prevalence and clinical significance of routine screening for syphilis by ELISA for detection of *T.pallidum* antibodies in patients undergoing invasive procedures (surgical and percutaneous) at a tertiary care cardiac centre in India.

MATERIALS AND METHODS

The present study was a prospective study which was conducted at a tertiary cardiac care centre in India. All patients aged above 18 years undergoing surgical and percutaneous invasive procedures during the study period from March 2017 to August 2017 were screened. The study protocol was approved by the institutional ethics committee. Written informed consent was obtained from all patients. The sera of patients were tested with third generation double antigen sandwich ELISA for the detection of immunoglobulin G (IgG) antibodies to *T.pallidum* [12,13]. The assay consisted of microwell strips precoated with recombinant 47 Kd and 17 Kd *T.pallidum* antigens conjugated to Horseradish Peroxidase (HRP). Samples along with positive and negative controls were added in the coated wells and incubated simultaneously with antigen HRP conjugate. The wells were washed to remove unbound components and captured antibodies were detected by adding substrate. The absorbance was determined for each well at 450 nm with an ELISA reader. The absorbances of all the wells were compared with the cut-off value provided by the manufacturer. Any sample having absorbance more than the cut-off value was considered positive.

All patients who were positive for ELISA were confirmed with *Treponema pallidum* Haemagglutination Assay (TPHA). The qualitative TPHA test was performed, wherein an even layer of agglutination was interpreted as a positive reaction, while a compact button was interpreted as a negative reaction. Agglutination in both the control cell well and the test cell indicated the presence of nonspecific agglutination in the sample and the test was considered invalid [13].

The patients were also screened for HIV, HBV and HCV using rapid test. The results of the tests were informed to the treating surgeons and cardiologists before the procedure. All patients with positive ELISA and TPHA test were evaluated for clinical features of syphilis.

RESULTS

A total of 13,865 patients were screened over a period of six months. Sixty-four patients were positive for ELISA of which 63 patients were confirmed by TPHA, which represents 0.45% of the patients screened. The specificity of ELISA was 98.4%. The age group of patients and other baseline characteristics are summarised in [Table/Fig-1]. Majority of patients were in the age group of 51-70 years (71.4%) and were predominantly male (76.2%). The most common clinical indication for an invasive procedure was Ischaemic Heart Disease (IHD), which included both acute coronary syndrome and stable IHD (68.2%). Three patients had manifestation of cardiovascular syphilis of which two patients had ostial coronary artery stenosis and one patient had aortic aneurysm with moderate aortic regurgitation. Among the patients screened for syphilis, two patients were positive for HIV also. One patient was newly diagnosed and the other was a previously diagnosed case already receiving anti-retroviral therapy. None of the patients were positive for HBV or HCV. [Table/Fig-2] represents the type of invasive procedures performed.

	Number (%)
Age distribution (in years)	
<40	3 (4.8)
41-50	11 (17.5)
51-60	25 (39.7)
61-70	20 (31.7)
71-80	3 (4.8)
>80	1 (1.6)
Sex distribution	
Male	48 (76.2)
Female	15 (23.8)
Clinical indication for procedure	
Ischaemic heart disease	43 (68.2)
Valvular heart disease	11 (17.4)
Peripheral artery disease	3 (4.7)
Complete heart block	4 (6.3)
Cardiomyopathy	2 (3.1)
Cardiovascular Syphilis	3 (4.7)
Other serological test	
HIV	2 (3.1)
HBsAg	0 (0)
HCV	0 (0)

[Table/Fig-1]: Baseline characteristics of the patients.

	Number (%)
Total	61
Percutaneous	49 (80.3)
Surgical	12 (19.7)
Percutaneous procedures	
Coronary Angiogram	22 (36.0)
Coronary Angioplasty	20 (32.8)
Peripheral Vessel Angioplasty	1 (1.6)
Pacemaker Insertion	4 (6.6)
Balloon Mitral Valvotomy	2 (3.3)
Surgical	
CABG	7 (11.5)
Valve Replacement/Repair	5 (8.2)

[Table/Fig-2]: Procedures performed on patients.

Universal precautions were followed by the operators during all procedures. There were no reported events of needle prick or mucus membrane exposure to blood products during the procedures.

DISCUSSION

There is a paucity of data related to the prevalence of syphilis in the general population and in patients undergoing invasive procedures in India. Most data of syphilis seroprevalence is available from blood donor screening, pregnancy and Sexually Transmitted Infection (STI) clinics [6,14]. As per the Centre for Disease Control and Prevention (CDC) data of 2017, the incidence of syphilis infection in USA has increased from its nadir in 2000-2001 of 2.1/100,000 to 7.5/100,000 the highest reported since 1994 [3]. The seroprevalence of syphilis reported in India in pregnant women ranges from 0.57-0.78% [14,15] and in STI clinics it is about 2.6-3.4% [6,14]. There is no significant data available about the seroprevalence of syphilis in patients undergoing invasive procedures in India to the best of our knowledge. The seropositive rate of syphilis in our study was 0.45% which is lower than that reported in pregnant women or from STI clinics. Currently, there are two diagnostic algorithms for syphilis. The traditional one consists of initial screening with an inexpensive nontreponemal test (VDRL or RPR), followed by retesting reactive specimens with a more specific treponemal test-TPHA or the Fluorescent Treponemal Antibody Absorption (FTA-ABS) test. Quantitative nontreponemal tests are used to monitor responses to treatment or to indicate new infections. In the other reverse algorithm, treponemal test is used as the initial screening test, followed by a nontreponemal test. Though more timely, the reverse algorithm has a false positive rate of 14-40%. A second treponemal test is required to determine the clinical action needed [14,16]. An ELISA for detection of IgG antibodies to *T.pallidum* has a sensitivity of 98.4% and a specificity of 99.3% [17]. ELISA for detection of IgG antibodies was used in the present study for screening and the specificity was 98.4%. Owing to the low cost, ease of use and good performance, the use of rapid point of care treponemal tests is increasing [9]. Among the 63 seropositive patients in this study, only three patients had manifestation of cardiovascular syphilis. Two patients had ostial coronary artery stenosis and the other patient has aortic aneurysm with moderate aortic regurgitation. All patients who were positive for ELISA and TPHA in the present study were administered single intramuscular dose of 2.4 million units benzathine penicillin and advised consultation with venereologist. Most cases of syphilis are transmitted by sexual contact or congenitally. There have also been reports of transmission via blood products, organ donation and occupational exposure [10,18]. A rare case of seroconversion post needlestick injury has also been documented [19]. The overall risk of transmission after needlestick injury appears to be low. There was no reported incidence of accidental needlestick injury in this study. However, it is safe to follow universal precautions while handling syphilitic cases which carry risk of transmission through contact via cutaneous lesions and needlestick injuries [10]. Post-Exposure Prophylaxis (PEP) following sexual contact has shown to reduce the risk of transmission [20]. There is a paucity of data regarding benefit of prophylaxis post occupational exposure. It appears to be reasonable to consider prophylaxis post occupational exposure to minimise the risk of transmission based on benefits seen with post sexual exposure prophylaxis. The treatment of choice following sexual contact is benzathine penicillin (single dose 2.4 million units intramuscular) [10]. The alternatives to penicillin include tetracycline and doxycycline. Recently, single oral dose of doxycycline (200 mg) has been shown to be effective in reducing the risk of transmission [20]. There are no standard recommendations for serological testing post exposure.

LIMITATION

History of exposure to syphilis was not elicited from the patients. Routine testing of spouse and sexual partners was not performed in the study.

CONCLUSION

The seroprevelance of syphilis in the general population is very low. Routine pre-procedural screening may not be beneficial as it leads to added costs. However, screening may be considered in selected patients with clinical manifestations suggesting syphilis or with risk factors for developing syphilis or other STI.

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PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Microbiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India.
2. Assistant Professor, Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India.
3. Assistant Professor, Department of Microbiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India.
4. Professor, Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. KR Nishanth,
Sri Jayadeva Institute of Cardiovascular Sciences and Reserch, Bengaluru-560069, Karnataka, India.
E-mail: kr.nishanth@gmail.com

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