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A Review on Syphilis: Clinical Manifestation and Epidemiology

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Syphilis is a persistent infection caused by the bacteria Treponema pallidum prevalent in low-income countries but rare in middle- and high-income countries. T. pallidum is known for its invasiveness and immune evasion; its clinical symptoms are produced by local inflammatory responses to replicating spirochetes and are often confused with other diseases. The spirochete has a prolonged latent phase in which people might be infected even if they don't display any symptoms. Individuals, as well as the entire population, are affected by the sickness. Only one drug, penicillin, is recommended for the treatment of syphilis, and response to therapy is evaluated by changes in serological test titers over months. Despite the availability of simple diagnostic tests and the effectiveness of treatment with a single dose of long-acting penicillin, syphilis is emerging as a global public health problem. This is especially true among guys in high- and middle-income countries who have sex with men. Even though syphilis is a long-standing disease with well-established treatment ideas, diagnosis and therapy can be difficult due to the wide variety of symptoms and the difficulty of interpreting serological tests. The World Health Organization (WHO) has set a target of lowering syphilis incidence by 90% by 2030, but progress is slow. Countries can reduce the prevalence of syphilis by ensuring detection, treatment, and referral of infections by partners.

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1. INTRODUCTION

Treponema pallidum, which causes syphilis, is a prevalent illness that affects 10-12 million people globally each year. Early syphilis is associated with a high morbidity rate, and a thorough assessment of HIV transmission data indicates that it is a crucial facilitator of HIV transmission. With the discovery of HIV infection [1] and the subsequent revelation of high rates of HIV infection among persons with syphilis, there has been a renewed focus on explaining high rates of syphilis and HIV co-infection. Congenital syphilis is still a leading cause of stillbirth, illness, and death in children worldwide. Syphilis is still prevalent among MSM and other groups with multiple sexual partners, and it is likely to reemerge in heterosexual populations if public health precautions are not implemented. Syphilis infections in MSM are of particular concern since syphilitic lesions increase the risk of HIV infection and transmission.

2. MICROBIOLOGY

T. pallidum is a spirochete that measures zero.11 to 0.19 mm in diameter and 6.0 to twenty.0 mm in length. As a result, peers regularly use dark-discipline microscopy in scientific instruction. Endoflagella permits the microorganisms to move in a corkscrew pattern, rotating quickly around their longitudinal axis while flexing, bending, and snapping along their entire period. It is a choosy organism with pH and temperature optimum levels of 7.2 to 7. four and 30.0 to 37.zero°C, respectively. It's immediately inactivated by moderate warmness, bloodlessness, and most disinfectants [2-3].

2.1 Clinical Manifestations

Syphilis, if left untreated, is a chronic illness that develops through several phases, each with its own set of symptoms and pathology.

2.2 Primary Syphilis

Primary syphilis, the earliest degree of venereal syphilis, appears three weeks after exposure and includes a painless number one chancre that usually seems on the genitals and clears on its very own within a few weeks if left untreated. The chancre is frequently undetected with the aid of the affected person, and syphilis might not be recognized till secondary syphilis signs and symptoms seem. The main level lasts for four-6 weeks, or till the chancre heals.

Direct contact with infected lesions is required for the sexual transmission of syphilis. Syphilis influences 30% of persons with sexual touch with an inflamed companion. Edematous and invaded by inflammatory cells, the skin around the initial lesion or chancre at the entrance point is edematous. The chancre core is mucoid and surrounded by a mononuclear cell infiltration; the chancre base is fibrotic and neovascularized and contains host-produced hyaluronic acid and chondroitin sulfate. The lesions may go away on their own after 1–5 weeks if they are present. The inguinal lymph nodes may grow somewhat during the early stages, although rarely uncomfortable. The lesion's serious contents include many treponemes. Antibodies to the chancre are seldom identified until 1–4 weeks after the chancre has formed, according to nontreponemal and treponemal syphilis serological assays [4].

2.3 Secondary Syphilis

The illness progresses to secondary syphilis. This stage generally follows the main stage by three months [3].

In the second stage of syphilis, the bacterium has infiltrated almost all bodily organs and fluids. Pyrexia, pain in the head, Pharyngitis, arthralgia, and anorexia are common nonspecific symptoms that appear 1–5 weeks after the original lesion has healed. Secondary syphilis, on the other hand, is characterized by a widespread rash, mucous patches, and hypopigmented, macerated papules.

Leukocyte infiltration, keratinocyte necrosis, epithelial cell thickening, and variable degrees of hyperkeratosis are some epithelial abnormalities identified in these lesions. These symptoms generally go away on their own after 2–6 weeks, but if the patient is not treated, they may return throughout the first year of infection. Immune complexes fabricated from IgG and C3 that flow the bloodstream and are recognized in spherical eighty% of all secondary cases can result in an immune complex deposition in the kidneys and subsequent renal injury. In certain patients, secondary syphilis, on the other hand, might lead to neurosyphilis and cardiovascular syphilis [5-7].

2.4 Latent Stage

The illness typically enters a latent stage after the secondary level, while it may remain nearly inactive in a man or woman's device for 10 to twenty years or greater, and in some individuals, indefinitely. The proportion of individuals who relapse and once they relapse are used to categorize latent syphilis into early and past due stages. Early latent syphilis is defined as asymptomatic syphilis lasting as much as three hundred and sixty-five days, while past due latent syphilis is defined as asymptomatic syphilis lasting more than one 12 months [5]. Patients with latent syphilis may expand secondary syphilis, stay asymptomatic within the latent stage, or increase tertiary syphilis [8-9].

2.5 Tertiary Stage

Venereal syphilis' 1/3 degree is the maximum superior, with signs growing as much as forty years after the primary infection. Approximately 1 / 4 of men and women with untreated syphilis develop tertiary syphilis. It is turning into increasingly more much less widely widespread in most regions of the sector where treatments are comfortable to be had. Severe and perhaps fatal symptoms mark this stage. Neurosyphilis and cardiovascular syphilis are the most frequent tertiary syphilis symptoms. Treponemes infiltrate the cerebrospinal fluid, causing neurosyphilis. Patients may experience no additional symptoms at this stage, but others may develop syphilitic meningitis. Patients may develop meningovascular syphilis, tabes dorsalis, or paresis as a result. Scientific symptoms of dementia and psychosis, as well as irritability and character abnormalities, characterize paresis. Cardiovascular syphilis accounted for a large percentage of normal clinical cardiovascular contamination, and a large variety of syphilitics had cardiovascular abnormalities at post-mortem. The most unusual issues are syphilitic aortitis (infection of the aorta) and aortic regurgitation (blood leaking from the aorta returned into the left ventricle). this will bring about pain, anguish, and even cardiac failure [10].

2.6 Congenital Syphilis

Because the organisms directly infect the fetal blood, the initial stage of the illness is not visible in congenital syphilis. It's possible that necrotizing funisitis is present or not. Treponemes, or their consequences, can be observed in almost every infant's tissue. IgG antibodies passively transmitted from the mother to the child are measured through widespread syphilis serological assessments, not IgM antibodies generated by the infant for the duration of being pregnant. Physical, radiographic, serological, and direct microscopic investigations are presently used to diagnose new child congenital syphilis.

Although specific clinical manifestations are evident from birth, they are most commonly encountered between the ages of 3 and 6 months. as much as 50% of toddlers with congenital syphilis are asymptomatic at birth, and different symptoms together with enamel and bone deformity, listening to impairment, vision loss, and getting to know impairments can also seem later [8-11].

2.7 Epidemiology

According to the latest World Health Organization predictions, 7 million new syphilis infections will occur globally in 2020. Between 2000 and 2020, the global cumulative frequency of syphilis among guys who had sex with men was 7.5 percent. (95 percent confidence interval: 7.08.0). According to new estimates, there are 355,000 cases of poor birth outcomes, accounting for a significant share of newborn fatalities and illnesses. The worldwide burden of congenital syphilis dropped from roughly 750,000 to 660,000 between 2012 and 2016, although the decline was not substantial [12].

In December two thousand nineteen, a novel form of coronavirus (CoV) was discovered in Wuhan. The virus spread fast worldwide through human-to-human contact, quickly becoming a pandemic. Primary (fever, cough, dyspnea) and secondary (loss of smell, taste disorders, headache, gastrointestinal symptoms, skin lesions) symptoms are distinguished. Since then, it has wreaked havoc on social and economic systems worldwide. There is currently no anti-COVID19 antiviral medication that is clinically useful and recognized (Remedies have shown excellent results, but further discussion is needed). Researchers are still working on new medications and vaccines.

Researchers have been trying to figure out the virus's genetic diversity since the outbreak began, looking for things like changes in immunological targets (glycoproteins), variations

in primer and probe binding sites (limit diagnostic test sensitivity), and genetic variety (which may impact infectivity & virulence).

Different variants comprising nucleotide deletions in ORF8 have been discovered, and the wild type. The 382 variant (deletion in ORF7b and ORF8), which removes their transcriptional regulatory sequence, is the most well-known (this omission will prevent ORF8 transcription). Early in the outbreak, this variation propagated successfully, although it was not recognized until March 2020. These various varieties have been discovered in places around the world, including Bangladesh (three hundred forty-five nucleotides), Australia (one hundred thirty-eight nucleotides), and Spain (sixty-two nucleotides). A passenger returning to Taiwan from Wuhan, China, identified the same 380 version in February 2020.

During the last pandemic in 2002-2003, SARS-CoV caused zoonotic diseases from civet cats to humans. The wild-type virus mutated soon after& a new strain emerged. It contained a 29-nucleotide deletion in ORF8, dubbed 29. A deletion of 82 nucleotides and 415 nucleotides in the same area was discovered. Pandemic's impact on these weaknesses is not clear. In vitro studies have revealed that the replication efficiency of 29 is lower than the wild type and that the clinical sickness is milder.

Syphilis is one of the most prevalent sexually transmitted illnesses globally, with about 6 million new cases each year. If a pregnant woman becomes sick and does not receive prompt and adequate treatment, the illness will spread to her fetus. Low birth weight, preterm birth, and other birth abnormalities are all possible outcomes.

Despite a decrease between 2012 and 2016, the number of pregnant women and newborns impacted remains unacceptably high. For a pleasant pregnancy experience, all women should receive early syphilis screening and treatment as part of high-quality prenatal care.

The World Health Organization (WHO) has set a 90 percent reduction in syphilis infections by 2030, but progress is slow. Countries may aim to minimize syphilis prevalence by ensuring that infections are detected, treated, and referred to partners [6]. Investing in public health infrastructure and human resources, boost testing and routine screening, ensure a steady supply of drugs, treat found cases, support partner therapy, and develop new methods like preventative medication and vaccines [13-18].

3. LAB DIAGNOSIS

Treponema pallidum causes syphilis, a persistent infection with various clinical symptoms that appear at different stages. Treponema pallidum has been stained with a basic laboratory dye for many years since it is difficult to cultivate (7,8). Other laboratory techniques for identifying the various phases of syphilis infection have been developed. There are four types of syphilis testing available:

(i) Direct microscopic examination, which is utilized when lesions are present; (ii) Non-treponemal test for screening; (iii) Confirmatory treponemal test; (iv) Direct antigen detection test, which is now being used in the research setting.

3.1 Direct Microscopic Examination

While lesions are apparent, direct identification of the bacterium is the most precise and easy method of diagnosing syphilis. On microscopispection, an excellent result is conclusive proof of syphilis if different pathogenic treponemes have been dominated out. Darkfield imaging also can detect number one syphilis several days to weeks earlier than reactive serologic tests seem. Then again, a poor direct microscopic result does now not rule out the capability of syphilis. There may be too few organisms to investigate because the lesion is healing or the spirochete has been modified via systemic or topical treatment.

3.2 Darkfield Microscope

This technique stays one of the only and most dependable for detecting T pallidum directly. Moist mount dark-field microscopy is used to look at exudates and fluids from lesions. T pallidum may be recognized from different spirochetes through its shape and motility. This technique works excellent when the lesions are wet, and the inspection may be adequately executed after the fabric is gathered. Even though the presence of T pallidum is the gold preferred for analysis, darkish-discipline microscopy has low sensitivity, and the absence of T pallidum does no longer rule out syphilis.

3.3 The Direct Fluorescent Antibody Test for T Pallidum

The direct fluorescent antibody tissue test detects T pallidum in tissue sections and may be used with historical, logical staining to screen for pathogenic Treponema spp. in biopsy and autopsy material.

The DFA-TP uses an antigen-antibody response to identify and distinguish pathogenic treponemes from nonpathogenic treponemes; hence, the organism does not need to be motile [19-20].

3.4 Serology Test

Serological checks are the maximum well-known manner of diagnosing syphilis. Those checks search for antibodies to lipoidal antigens that propose contamination (nontreponemal strategies) or antibodies to precise treponemal antigens (treponemal strategies).

3.5 Nontreponemal Tests

Nontreponemal assays may be used as qualitative screening exams or quantitative observation findings after remedy.

The VDRL slide, USR, RPR 18-mm spherical card, and believe currently seem popular nontreponemal checks [21]. Immunoglobulin M (IgM) and IgG antibodies to lipoidal material created from injured host cells, further to lipoprotein-like material and likely cardiolipin generated by treponemes, are measured in nontreponemal (reagin) assays [22]. Cardiolipin, cholesterol, and lecithin are measured in defined portions in the Venereal disorder studies Laboratory (VDRL) check. The most straightforward take a look that may be used to check CSF is the VDRL.

The presence or absence of antibodies is readily measured using undiluted patient serum in qualitative nontreponemal assays. The serum is diluted in repeated two-fold dilutions until an endpoint is met in quantitative nontreponemal testing.

Nontreponemal screening assays have the benefit of being widely available, inexpensive, and simple to run on large numbers of specimens and necessary for determining therapy efficacy.

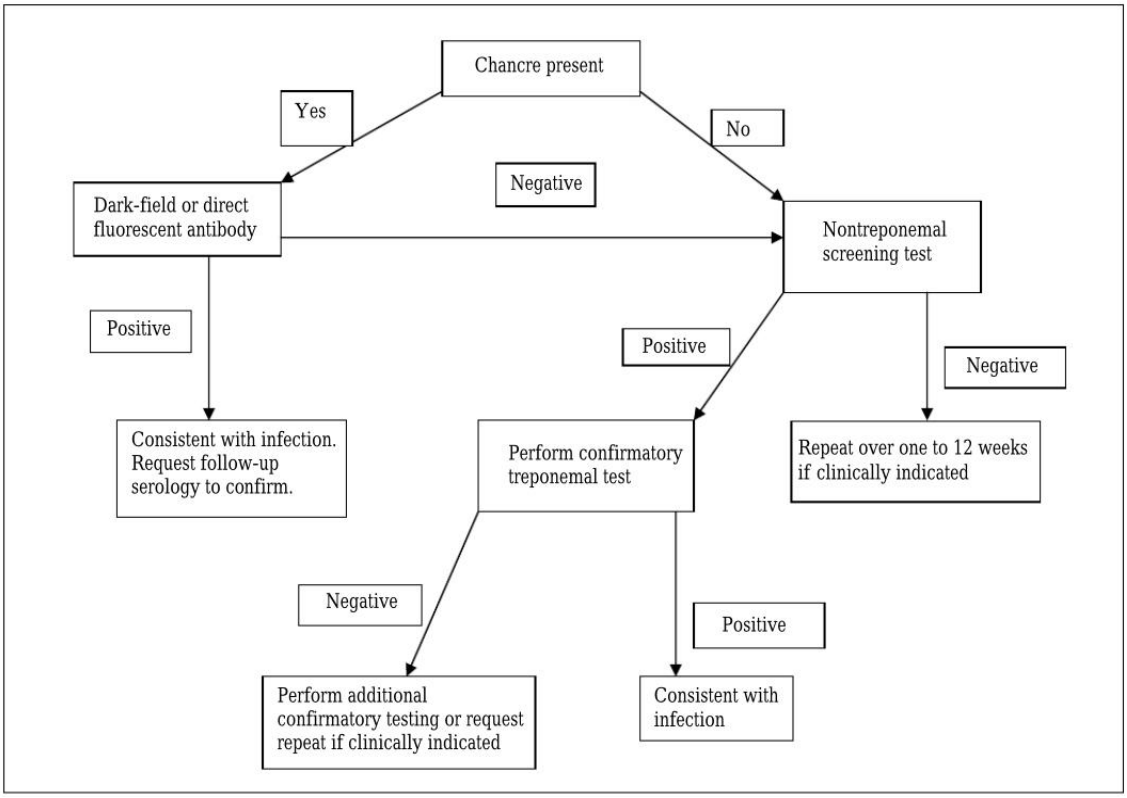

Fig. 1. Treponemal test

3.6 Treponemal Test

The FTA-ABS, FTAABS double staining, and MHATP tests are presently regarded as standard treponemal assays. These assays employ Treponema pallidum as the antigen and work by detecting antibodies to Treponema pallidum components [23-29]. The treponemal test is primarily used to confirm the non-treponemal test's responsiveness. When the non-spirochete test fails, the spirochete test can be performed to confirm the clinical impression of syphilis. However, in low-prevalence communities, the Treponema test can identify the illness using a fast test or an enzyme immunoassay (EIA) format. When utilized appropriately as a confirmatory test, treponema tests have practically no technical restrictions, but they do have economic constraints. The early phase 1 Treponema pallidum test's response varies. The phase 1 Treponema pallidum test's various sensitivities are related to the period of serum collection after the illness has developed.

4. CONCLUSION

The World Health Organization (WHO) has set a target of lowering syphilis incidence by 90% by 2030, but progress is slow. Countries can reduce the prevalence of syphilis by ensuring detection, treatment, and referral of infections by partners.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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