

Increasing Trends of Syphilis and Histopathological Correlates: Study in a Tertiary Care Centre in India

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Abstract: Background: Syphilis is a venereal disease with multisystem manifestations resulting from infection with bacterium *Treponema Pallidum*. (1) Syphilis is categorized as Primary, secondary, tertiary and Congenital forms. (2), (3). We aim to expose the increasing trend of this bygone malady and how histopathology can sometimes not only aid in confirmation but diagnosis of a clinically unsuspected case. Syphilis has come to the limelight as a public health hazard as seen in our centre. Aims: To find out the rising trends in the presentation of syphilis and to analyze the histopathological clues for the diagnosis in skin biopsies. Subjects and Methods: We analyzed the case records of all cases of STDs with special emphasis on Syphilis registered in the department of Dermatology and Venerology. A diagnosis of Syphilis was predominantly made based on clinical and serological grounds. However, in some, histopathology of skin proved to be path breaker in the diagnosis of this great mimic. Here in we analysed the histopathological characteristics of the same. Results: Among the STI cases examined the most commonly found STI was Syphilis (57%) followed by Genital warts (22%). 70% were Males and 79% were in the age group of 21-30 years and least in the 81-90 years (0.05%). 3 cases (1.51%) were of congenital syphilis Syphilis had varied skin manifestations at various stages detected by Histopathological examination. Implication of the study: Syphilis is a systemic disease caused by the spirochaete *Treponema pallidum* (TP) and is one of the oldest known diseases. It has now re-emerged as a cause of public health concern in the modern-day world. Syphilis causes histologic features of the affected tissue depending on the type of lesion and the stage of the disease. We have seen that some cases could have come to the limelight in the era of Covid -19 pandemic in an other unsuspected case and there has been an increasing trend in the post covid era.

Keywords: Syphilis, rising trend, histopathology

1. Introduction

Syphilis is a sexually transmitted disease (STD) caused by *Treponema pallidum* (*T. pallidum*). The causative organism was first discovered by Fritz Schaudinn and Erich Hoffmann in 1905 (4). *T. pallidum* is a motile spirochete that is a helically coiled, corkscrew-shaped which is 6 to 15 µm long and 0.1 to 0.2 µm wide. (5). The spirochete has a slow metabolic rate, with an average multiplication rate of 30 hours. *T pallidum* is the only treponemal agent that causes venereal disease. (6) Man is the only definitive host.

Transmission

It is estimated that 30-60% of sexual contacts of cases with early syphilis will acquire the disease themselves and mostly the spirochete is inoculated through foci of microtrauma usually inoculated through microtrauma usually mucosal membranes (7).

Stages

The lesion of primary syphilis occurs at the site of inoculation of the spirochete. Commonly seen as single and painless but can be multiple and painful. Usually, the lesion starts as a macule that becomes a papule, which then ulcerates. A two-to-three-week incubation period usually happens between the inoculation of *T pallidum* and development of the lesion (the range of incubation period is reported as being 9-90 days). Local, non-tender lymphadenopathy is often an accompaniment of this lesion. If left untreated, the lesions spontaneously heal after 4 or 5 weeks. Four to eight weeks after the primary stage, it becomes a systemic infection with bacteraemia. This secondary stage of syphilis is characterised by a generalised and usually symmetrical macular papular rash, which is usually generalised and may involve the palms, soles and back. (8). Histopathological examination is usually sought for these lesions in the secondary stage. Secondary

stage is also characterised by vasculitis which can cause hepatitis, iritis, nephritis, and neurological problems. The tertiary phase is rare and is commonly seen in poor countries (9, 10).

Detection: Direct methods such as Dark field microscopy, PCR and fluorescence antibody testing may be used but not widely available. (19) The advantage of dark field microscopy is that the spirochete can be detected even before serological tests become positive. (18) Serological tests include Treponemal and non-treponemal tests. Treponemal tests (fluorescent treponemal antibody absorbed (FTA-ABS) test, and chemoluminescence immunoassays and enzyme immunoassays) detect antibodies to the spirochetal proteins. Nontreponemal tests detect antibodies which is aimed against lipoidal antigens, damaged host cells, and possibly from treponemes. (19)

Global Trends

The worldwide incidence of syphilis increased from 8, 845, 220 (95% UI: 6, 562, 510–11, 588, 860) in 1990 to 14, 114, 110 (95% UI: 10, 648, 490–18, 415, 970) in 2019. The global Age standardized Incidence rate (ASIR) continued to increase profoundly, especially from 2010 to 2019. In a study inclusive of 21 countries South Asia recorded the highest number of incident cases at 2, 332, 440 (95% UI: 1, 691, 290–3, 098, 810) in 1990, and Australia recorded the lowest number of incident cases at 14, 100 (95% UI: 10, 460–18, 960) with central sub-Saharan Africa having the highest burden. (11)

Histopathology

The histopathological features of syphilis, which is most evident in secondary stage shows a wide spectrum, from interface dermatitis to granulomatous disease (13-16).

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2. Methods

To find out the rising trends in the presentation of syphilis and to analyze the histopathological clues for the diagnosis in skin biopsies we selected a retrospective cohort of patients diagnosed with Syphilis (in all stages) based on serology, clinical findings and in certain cases with aided histopathological correlation of the skin lesions. The study was conducted in the Department of Pathology of Amrita Institute of Medical Sciences (India). Number of cases of Sexually transmitted diseases were collected from the department of Dermatology and Venereology from January 2016 till October 2023. (414 cases out of which 235 were cases of syphilis). Sample size was calculated with proportion score as cited by Palanisami et.al (12) was calculated as 78. Serology positive cases (tested using RPR, VDRL titres) of Syphilis were also collected from department of Microbiology and correlated with the data.

3. Results

Among the STI cases examined the most commonly found STI was Syphilis (57%) followed by Genital warts (22%). (Figure. 1)

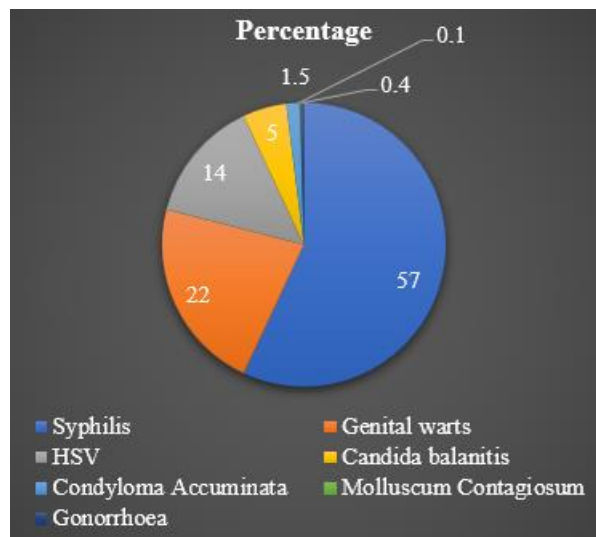
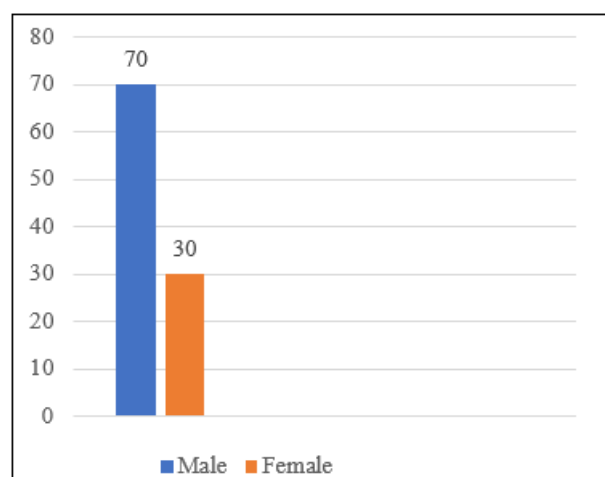


Figure 1

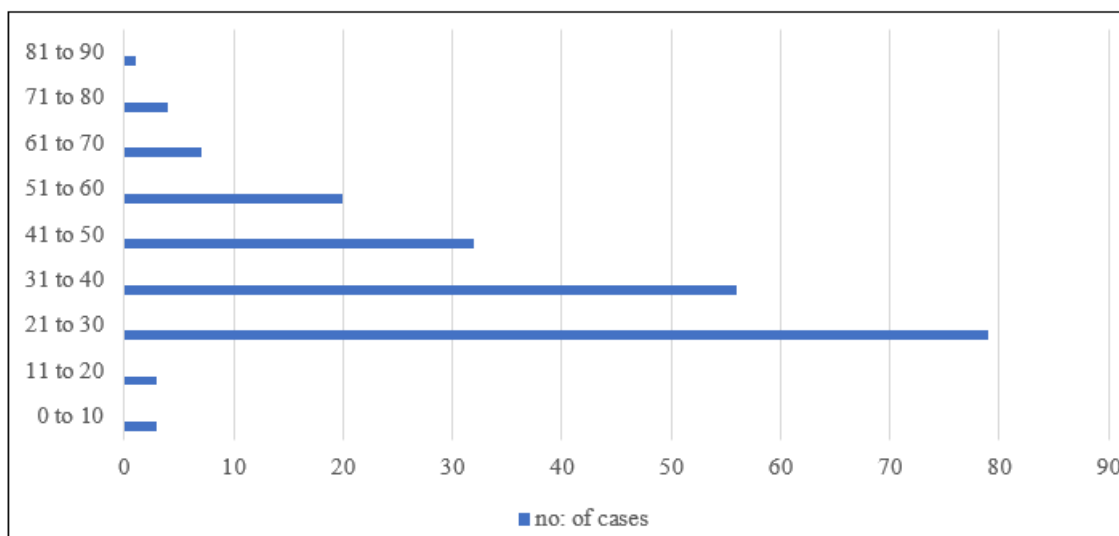
Gender Prediliction:

Predominant population affected were males (70%)



Age range:

79% were in the age group of 21-30 years and least in the 81-90 years (0.05%).



Syphilis had skin specific and non-specific skin manifestations at various stages detected by histopathological

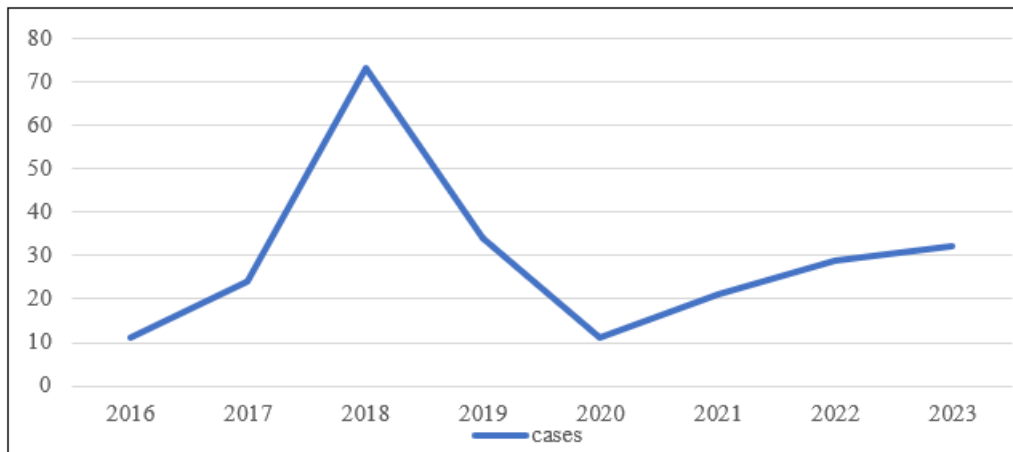
examination. Lichenoid superficial and deep perivascular and periadnexal lymphohistiocytic inflammation with admixed plasma cells was the predominant pattern observed

A subset showed psoriasiform dermatitis and granulomatous inflammation.

Incidence:

In our case there has been an increasing trend starting from the year 2017 with peak cases in late 2018 followed by a fall in 2020 and an increase in 2021 there after showing a steady increase till date.

3 cases (1.51%) were of congenital syphilis. 5 of the cases had skin lesions that were examined histopathologically.



Histopathological aspects:

Skin biopsies received in the Department of Pathology of Amrita Institute of medical sciences and Research centre were paraffin embedded and microscopic sections were examined and most of the cases show irregular acanthosis with dense dermal infiltrate predominantly composed of plasma cells.

Vasculitis of the dermal capillaries were also observed. (Fig.5) One of the biopsies received were not clinically diagnosed as a case of secondary syphilis but was confirmatory of the same pathologically which later on was serologically confirmed as a case of secondary syphilis.

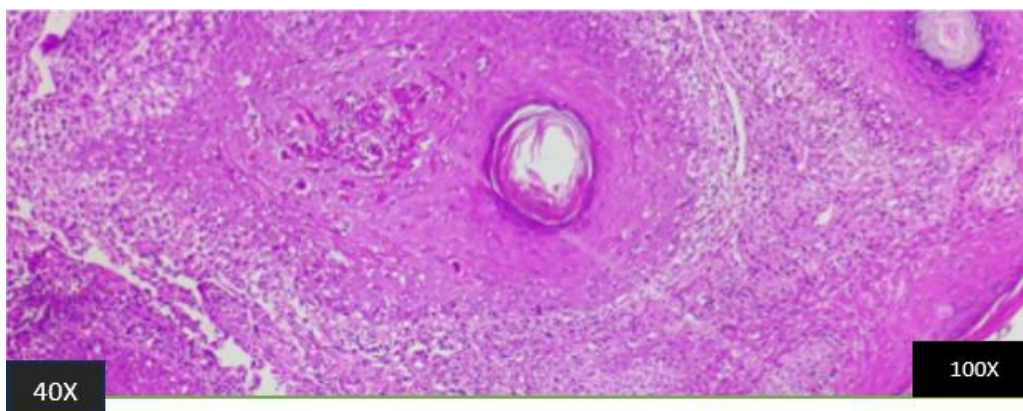
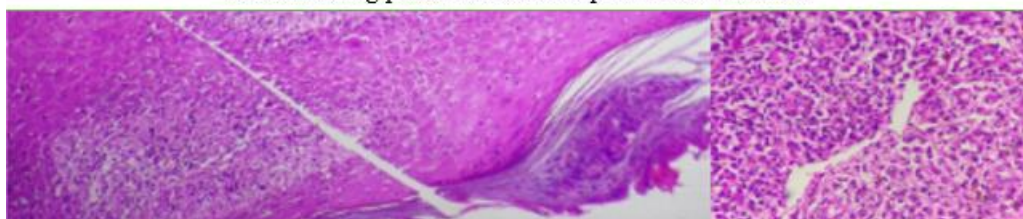


Figure 5: Dilated hair follicles and dense dermal inflammation composed of plasma cells. Inset showing perivascular dense plasma cell infiltrate



4. Discussion

Syphilis appears to be in the era of re emergence as it appears to be the most common sexually transmitted disease among the venereology case records examined. (12) In our case there has been an increasing trend starting from the year 2017 with peak cases in late 2018 followed by a fall in 2020 and a second peak in 2021 there after showing a steady increase till date. We

assume that some cases could have come to the limelight in the era of Covid -19 pandemic in an other unsuspected case as is seen in a study done by Anaya Sambyal Et.al (17). Congenital syphilis incidence was 1.5%. Majority of cases were males (70%) and in the age group of 21-30 years (79%) as is similar to the references from Kojima et.al (20). The histopathological findings of skin lesions consisted of lichenoid and psoriasiform dermatitis and granulomatous

inflammation. In sometimes unsuspected cases of clinical cases, histopathological examination of skin lesions paved the way to further testing and confirmation of the diagnosis. We however did not have data on homosexual males.

5. Conclusion

The study conducted in our institute showed a resurgence of Syphilis which appears to be of public health significance as it appears to be one of the most common Sexually transmitted diseases among the young population predominantly in males with varied dermatopathological findings. Suspicious histopathology may help aid clinicians to test for a case as was the case in one of our cases. The possible reasons for the recent increase in the prevalence of syphilis, mentioned in various studies, include an increased frequency of penooral and penoanal sex and an increased frequency of Males having sex with males and HIV coinfection (20).

The incidence of congenital syphilis in our study was 1.5% and hence robust screening of cases using VDRL/RPR in dilution need to be done instead of non-specific dilution methods that are being routinely done. Syphilis screening and prompt treatment amongst risk groups have become crucial along with proper surveillance and public health measures to prevent disease transmission as these cases may have heterogenous clinical presentations even among venereologists among other medical and surgical specialities.

Lack of adequate and timely treatment may ultimately lead to tertiary syphilis, recurrence of the highly infective phases, and also continuous transmission of infection. Scaling up the case finding in the early phases is the need of the hour. A high index of suspicion, a rapid card test for screening, and sensitizing the other medical fraternity about the disease is of imminent importance.

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