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Clinical Epidemiological Study of Secondary Syphilis - Current Scenario

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Abstract:
Introduction: *Sexually transmitted infections (STIs) are a major global cause of acute illness, infertility, long term disability and death, with severe medical and psychological consequences for millions of men, women and infants.[1.]Prevalence of sexually transmitted infections shows variations from country to country and in different settings. There were many reports about upsurge of syphilis after 2005 more so in MSMs and in association with HIV was also increasingly observed.*
Objectives:*To determine epidemiological data of secondary syphilis cases, to determine the association between Secondary syphilis and HIV and MSM activity.*
Methodology: *During the study period (January 2013 to October 2015) all the suspected cases of secondary syphilis were interviewed and examined in detail, blood collected was screened for Syphilis (by RPR, TPHA), Hepatitis Band , HIV. Data analyzed.*
Results: *Out of 1,76,856 patients who attended DVL OPD, 54 cases were diagnosed as having secondary syphilis. In 2013 the cases were 6, 2014 they were19, in 2015 till October were29. Among the 54 cases 48 were males, 28 of them had associated HIV infection, 32 of 48 males had homo or bisexual activity. Majority had multisystem involvement and one pregnant woman had condylomatalata lesions. Five patients showed prozone phenomenon. Two cases showed high dilutions in both RPR (1:512dil, 1:1024 dil)andTPHA was positive. None of them showed any C.S.F. changes suggestive of asymptomatic Neurosyphilis. All the Patients responded to standard treatment given.*
Conclusion: *Year wise increase in number of secondary syphilis cases was observed. Among these 88.89% were males, 51.85% had HIV association, 66.66% of males had history of homo and bisexual activity. As co-infection is frequent, therefore, all patients with syphilis should also be screened for HIV infection and vice versa Multi-centriclong duration studies are needed to prove the upsurge of syphilis.*
Key words: *Secondary syphilis RPR TPHA HIVinfection MSMs*

I. Introduction:

Sexually transmitted infections (STIs) are among the most widespread and harmful infectious diseases. The epidemiological profile of STIs is more dynamic than that of other diseases. An estimated half a billion new curable STIs occur worldwide each year(WHO report 2014)[1],[2.] STIs are also among the 5 leading causes of health problems in developing countries. Syphilis, Gonorrhoea and chlamydial infections cause morbidity and mortality though curable with Antibiotics. Viral STI`s, Human Herpes Simplex Virus (HSV), Human Papilloma Virus (HPV), Hepatitis B Virus (HBV) and Human Immunodeficiency Virus (HIV) more commonly seen now a days but incurable (estimates remain imprecise). Multiple STIs occur commonly facilitating the increased transmission of HIV by sexual route.Prevention and control of these infections involve strategies, to reduce sexual transmission. The world Health organization (WHO) laid down Global Strategy for the prevention and control of sexually transmitted infections in 2006-2015 ``Breaking the chain of Transmission `` [2]showed the Key strategies and effective interventions among the High Risk group (HRG) to prevent STI and to slow down the overall transmission. Reliable data was required to guide an effective response in this regard.

Syphilis was a sexually transmitted infection (STI) of considerable public health importance due to both its global reach and its associated complications and sequelae.[3,4]Syphilis caused by a Spirochete T.pallidum sub sp. pallidum, in its primary stage causes genital ulceration, a strong co-factor for HIV acquisition and transmission. Case reports of primary and secondary Syphilis were an important source of information about new cases of Syphilis. Until 2013, Syphilis data was not routinely collected at Global level, but now included in GARPR, from all regions. Most infectious stages of Syphilis (Primary& Secondary) incidence decreased throughout the world from1992 -2000(all time low).Recent epidemiological studies in Europe, the USA and Australia have shown that the number of syphilis cases had been increasing[2,5-7]. In India viral STI predominantly reported over bacterial STIs in different studies, may be because of the indiscriminate and prophylactic use of over-the-counter broad-spectrum antibiotics, up-gradation of health services at the primary level and the success

of 'syndromic' approach of treatment, has resulted in major changes in epidemiological patterns.[8]Syphilis was observed as commonest and at slightly increased rates in most of the reports. CDC research estimated that more than half of syphilis cases occurred in Men having sex with Men (MSM) in recent years. The increase in syphilis among MSM is a major public health concern, particularly because syphilis and the behaviors associated with acquiring it, increase the likelihood of acquiring and transmitting human immunodeficiency virus (HIV). There were reported rates of 50%–70% HIV co-infection among MSM infected with primary and secondary syphilis.[9]In men it was observed 6 times more than in women. The increase in the concordant Human Immunodeficiency virus (HIV) infection and syphilis observed by clinicians over the past decade,has renewed interest in this field as their interaction is complex.Syphilis manifests similarly in HIV infected and HIV uninfected patients with minor difference. In HIV infected Primary Syphilis may manifest with more than 1 chancre and nearly 1/4th of them present with concomitant lesions of primary and secondary Syphilis. Atypical and aggressive Syphilitic lesions occur more frequently among HIV infected but in a minority of cases. There is an estimated 2- to 5-fold increased risk of acquiring HIV if exposed to that infection when syphilis is present[10]

Fortunately T. pallidum is sensitive to penicillin and its devastating consequences are largely avoidable if the diagnosis is made promptly. Despite the availability of effective treatment and the potential for prevention, syphilis remains a major scourge of the modern world. Strengthening STI control can thus deliver broad and important public health benefits, contributing to the Millennium Development Goals (MDGs) for child health, maternal health and HIV(WHO report 2014). In the context of above observations a clinical-epidemiological study of cases of Syphilis in particular secondary syphilis attending DVL department of a tertiary care hospital in Telanganahas been taken up.

II.Objectives:

To find out the epidemiological data of Secondary Syphilis, To determine the association between Secondary Syphilis and MSM,To determine the association between Secondary Syphilis and HIV

III.Methodology

All the patients attending DVL OP of Gandhi Hospital, Secunderabad, Telanganaduring January,2013-October, 2015 were interviewed to getdetailed history, demographic data, examined in detailfor signs of secondary syphilis,and established diagnosis by Serological tests for syphilis (RPR, TPHA), HIV testing done in ICTC as per NACO Guidelines, HBsAg testing , Skin biopsy were done as and when necessary and data was analysed.

IV.Results

During the study period, 1,76,856 patients attended the DVL OPD, of these 54 cases were diagnosed as secondary syphilis clinically, confirmed serologically. In 2013-the cases were 6,in 2014 they were 19 and in 2015 they were 29(Table1).Out of the 54 cases 48 were males and 06 females with 8: 1 ratio, Common age group involved was 21 to 30 years, age range being 16 to 60(table 2).

Urban population consists of 55.55%,Rural44.44% (table 3). Among the males Unskilled workers were 37.5% followed by students (25%).83.3% of females were house wives (table 4). Twenty nine males were unmarried(60.42%), all the females were married (table 5). Twenty eight of them were having associated HIV infection (27 males and 1 female) shown in (table 6). Thirty two males with secondary syphilis gave history of either homosexual or bisexual contact (table 7). Majority of patients had multiple system involvement, Palmo plantar rash being commonest manifestation followed by lymphadenopathy and skin rash. Sixteen of them had condylomata lesions. One pregnant woman had only CondylomataLata lesions. None of these showed C.S.F. abnormalities (table 8). All the patients were reactive by RPR (five of them on dilution of serum) with 1: 8 to > 1:1024 dilutions range and were reactive for TPHA(table 9). Four of these patients had persistent primary chancre. A single dose 2.4 mega units of Benzathine Penicillin was given to all the HIV negative patients whereas PLHAs were given same treatment for 3 consecutive weeks. All the cases responded to the treatment, all skin and other manifestations disappeared within 4- 8 weeks, RPR titers dropped to less than 1:8 dilutions by 3-6 months whereas TPHA was positive throughout.

Table 1 Year wise Statistics of Sec. syphilis

Year	Total DVL cases			Sec. syphilis cases	
	Males	Females	Total	Males	Females
2013	28572	28212	56784	06	0
2014	29212	30692	59904	16	03
2015till Oct.	28736	31432	60168	26	03
Total	86520	90336	176856	48	06

Pie chart showing Male and female cases of Secondary syphilis

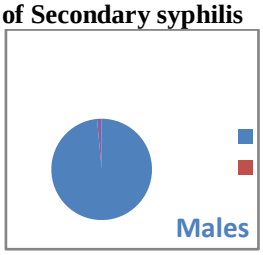

Table 2 Sex and Age Distribution of Secondary Syphilis cases

Age group	Males	Females	Total
<10yrs	0	0	0
11-20yrs	01	02	03
21-30yrs	33	04	37
31-40yrs	10	0	10
41-50yrs	02	0	02
51-60yrs	02	0	02
Grand total	48	6	54

Table 3 Sec Syphilis and Domicile

Sex	Urban	Rural
Males	26	22
Females	04	02
Grand total	30	24

Table 4 Sec Syphilis and Occupation

Occupation	Males	Females
Students	12	0
Hotel workers	03	0
Labourers	08	0
UnSkilled	18	0
Business	07	01
House wives	0	05

Table 5 Secondary Syphilis - Marital status

Age group	Married		Unmarried		Total
	Males	Females	Males	Females	
11-20yrs	0	2	1	0	3
21-30yrs	7	4	26	0	37
31-40yrs	8	0	2	0	10
41-50yrs	2	0	0	0	2
51-60yrs	2	0	0	0	2
Grand Total	19	6	29	0	54

Table 6 Type of Sexual contact Secondary Syphilis & HIV –Males

	With RVD	Without RVD
G-G	2	19
G-A	12	2
G-O	6	2
Multiple type	8	3

Table7 Secondary syphilis cases - Sexual Orientation Practices in Men

Age group	Hetero	Homosexual	Bi sexual
11-20	1	0	0
21-30	6	12	15
31-40	6	0	4
41-50	1	0	1
52-60	2	0	0
Grand Total	16	12	20

Table 8symptoms and signs of secondary syphilis

Symptoms or Signs of Sec. syphilis	PLHA with Sec. syphilis	Non-PLHA with Sec. syphilis	Total
Classical skin rash	14	18	32
Generalised lymphadenopathy	20	23	43
Palmo-plantar rash	22	24	46
Condylomatalata	12	04	16
Mucosal lesions	16	12	28
Split papules	04	02	06
Luesmaligna	02	01	03
Hepato-spleenomegaly	02	01	03
Eye lesions	01	00	01
Arthralgia/bone pains	10	04	14
Fever	08	04	12
Alopecia	04	06	10
PersistantPrimary chancre	03	01	04
Asymptomatic neurosyphilis	0	0	0
Alopecia	04	06	10

Table 9 Sec. syphilis and RPR correlation

RPR dilution	**With HIV**	**Without HIV**
1 : 8 dils	**04**	**05**
1:16	**03**	**03**
1 : 32 dils	**12**	**11**
1 : 64 dils	**08**	**06**
1:512	**0**	**01**
1:1024	**01**	**0**
Total	**28**	**26**

Skin Lesions

Oral And Cutaneous lesions among PLHA

Palmar rash

Split papules Condylomatalata lesions

V. Discussion

In spite of the availability of effective treatment, bacterial STIs are still a major public health concern in both industrialized and developing countries. This study showed increasing trend of secondary syphilis which was also the scenarioin the United Statesduring 2005–2013, where the number of primary and secondary syphilis cases reported each year nearly doubled, from 8,724 to 16,663; the annual rate increased from 2.9 to 5.3 cases per 100,000 population[2,9] In Ontario, Canada, reports of infectious syphilis rose from 0.4 to 5.9 cases per 100,000 from 2001 to 2012, with virtually all (96 %) cases among males [11.] In Russian federation also the largest increases were for primary and secondary syphilis in those aged 15 to 19 years[12.]In Asia, syphilis and HIV co-infection in China was also noted, a similar finding in which MSM was a high-risk population for both infections.[13]Various studies have shown a rise in the prevalence of syphilis in recent years in India[14]

This study consisted of 88.88% Men who outnumbered women11.12% in the ratio of 8:1 which was little higher than that observed by Anand BH et al from Bengaluru 75%and 25%,[15]Arpitha Jain etalas 70% and 30% respectively[16], probably because women report for investigations and treatment much later than men, due in part to the asymptomatic nature of the disease in women.A retrospective data analysis of one thousand STD patients from 1994 to 1998 at a Medical College, Trivandrum showed Males constituted 61.1% and females 38.9%.[17]

Among the men Secondary Syphilis was observed highest among unskilled workers followed by students. Factors associated with a high prevalence of syphilis include certain occupations such as long-distance truck driving and commercial sex work, presence of other sexually transmitted diseases (STDs), lack of male circumcision, and level of education.[18,19]

Urban population was slightly more than the rural among the study population which was also reported by WHO 2001(1)

Unmarried men were 60.2% having Homo and Bisexual activity, M&M weekly report of CDC stated that recent years have shown an accelerated increase in the number of cases, with the largest increases occurring among MSM.[9]This could be due to the behavioral changes of this population group, with a decrease in the preventive measurements and the increase of risky sexual practices that favor the infection.[20]HIV association was observed in 51.95% which was the scenario in US which reported rates of 50%–70% HIV co-infection among MSM infected with primary and secondary syphilis. The combination of syphilis and HIV is particularly dangerous because eroded secondary syphilids increase the risk of HIV infection, and HIV can alter the natural history of syphilis[21,22]

The resurgence of syphilis, coupled with its strong link with HIV, underscores the need for programs and providers to 1) urge safer sexual practices (e.g., reduce the number of sex partners, use latex condoms, and have a long-term mutually monogamous relationship with a partner who has negative test results for sexually transmitted diseases); 2) promote syphilis awareness and screening as well as appropriate screening for gonorrhea, chlamydia, and HIV infection; and 3) notify and treat sex partners[9]. Cross-sectional epidemiologic studies have demonstrated strong associations between evidence of past syphilis and HIV risk[22,23]

Maculopapular rash was the commonest manifestation followed by Lymphadenopathy which was also observed by Ameeta E Sing[24]Arpitha Jain[16].The typical lesion of the mucus membranes was the mucus patch, involving the tongue, buccal mucosa, and lips occurring in 5 to 22% of patients.Four patients (4/54) of the secondary syphilis showed persistent primary chancre, which Arpitha Jain[15], Asrul Abdul Wahab from Pakistan[25]also reported.

Alopecia was noticed in 10/ 54 Patients, which was found up to 7% of patients, alopecia characterized by patchy hair loss of the scalp, beard, and lateral eyebrows, which is referred to as a "moth-eaten appearance[26]

Luesmalignawas found in 3/54 cases in this study, two out of 55 patients was found in Chandigarh, India. Malignant syphilis was a rare form of destructive syphilide, with rupia-like ulcerative lesions and severe toxemia, which may end in death.[27] Ulcers, commonly seen over the face and extremitiesNo case of neurosyphilis was observed in this study which was in accordance with a retrospective analysis of the data obtained during 40-year study period from STI clinic attendees at a tertiary hospital inNewDelhi.All the cases responded well to standard treatment administered.

TPHA was positive in all the cases, RPR was reactive for 49 cases in undiluted serum and 5 were reactive after dilution. False negative results have also been reported with high-titer sera due to a prozone phenomenon.[28]Increased rate of negative serology test in both primary and secondary syphilis, increase false-negative non-treponemal antibody test due to prozone reaction, high rate of serological failure to clear non-treponemal antibody test after treatment and seroreversion to negative of specific treponemal antibody tests following treatment are commonly observed problems.[22] But in this study clinical(6 to 8 weeks)improvement and serological titer fall observed in3 to 6 months after treatment in all cases.

VI. Conclusion:

Year wise increase in number of secondary syphilis cases was observed. Among these 88.89% were males, 51.85% had HIV association, 66.66% of males had history of homo and bisexual activity. As co-infection is frequent, therefore, all patients with syphilis should also be screened for HIV infection and vice versa.
Multicentric long duration studies are needed to prove the upsurge of syphilis.

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