

Cystoscopic Biopsies of Bladder Neoplasms - A Snippet in Diagnosis

Bineeta Kashyap^{1*}, Nisha Goyal², Krishna Singha², Mohd Tajuddin³ and NP Singh²

¹Department of Microbiology, University College of Medical Sciences & Guru Teg Bahadur Hospital, Delhi, India

²Department of Microbiology, University College of Medical Sciences & Guru Teg Bahadur Hospital, Delhi.

³Department of Microbiology, Delhi State Cancer Institute, Delhi

ABSTRACT

Background & Objective: Despite the several ongoing campaigns highlighting the importance of safe sexual practices and public awareness activities about sexually transmitted diseases (STDs), syphilis still constitutes a significant public health problem in the developing countries. The present study was initiated to understand the current trend of syphilis among the (STD) clinic patients, patients receiving anti-retroviral treatment (ART) and antenatal mothers.

Methods: This study extended over a period of six years from 2013-2018. All the samples that were sent for routine VDRL testing were included in the present study. Samples were screened by qualitative and quantitative VDRL test.

Results: A total of 77,634 serum samples were screened for syphilis by VDRL testing over a period of six years. Out of these, 762 samples were reactive. Syphilis seroprevalence ranged from 0.33% to 2.19% with the highest seroprevalence in the year 2018. 75.6% of the cases belonged to 18-35 years age group. An overall upward trend of the VDRL reactive cases was recorded among all the three groups of STD, ART and antenatal clinic cases.

Conclusions: It is crucial to understand the current trend and epidemiology of syphilis among ART, STIs and ANC clinic attendees for the proper planning and implementation of preventive and control strategies.

Keywords: Syphilis; HIV; Sexually Transmitted Diseases; Antenatal Mothers; VDRL

Introduction

Sexually transmitted infections (STIs) particularly syphilis still constitute a significant public health problem in the developing countries like India. The repeated STIs and unprotected sexual behaviour have been shown to be strongly linked with HIV transmission.^{1,2} The prompt diagnosis and robust treatment of an STI can aid in reducing the risk of acquiring HIV infection in an individual. Despite the availability of effective treatment, various efforts to curb this disease often go in vain. Due to significant cultural barriers in Indian scenario, particularly women may hesitate in seeking STIs testing fearing the negative reactions from their family.³ Social stigma surrounding these STIs often leads to non-disclosure of the disease to the health personnel or in many cases these patients fall prey to local quacks who have their full trust.⁴ This poses a hindrance in the early detection and effective management of STI cases.

Syphilis is an infectious disease caused by the bacterium *Treponema pallidum*. It often manifests itself as a genital ulcerative disease. Syphilis and HIV share a complex association with each other.^{5,6} Syphilis enhances the risk of acquisition and further transmission of HIV infection by

increasing seminal viral load and viral shedding.⁷ Though the role of syphilis and HIV co-infection in the progression of HIV is still not clear, studies have reported that syphilis infection can cause a transient fall in CD4 counts and a surge in HIV viral loads.^{8,9} HIV also alters the disease presentation, natural course, management of syphilis in co-infection cases.¹⁰ Hence the emergence and propagation of HIV infection has further emphasized the importance of the early control of syphilis cases.

In developing countries, syphilis constitutes an important cause of preventable prenatal death.¹¹ Syphilis can manifest as low birth weight, preterm delivery, or even stillbirth. Mother to child transmission of syphilis may lead to congenital syphilis in the newborn.^{12,13} In order to limit these complications of syphilis WHO adopted a strategy for the actionable interventions to control the congenital syphilis in 2006. The targets for this strategy were to screen at least 90% first antenatal care attendees in the age group 15-24 years for syphilis and to provide adequate treatment to at least 90% syphilis-seropositive antenatal mothers by 2015.¹⁴ Despite the availability of effective tools for the diagnosis and prevention of mother to child transmission of syphilis, it continues to be a significant public health problem.

The control of syphilis is crucial to restrict the transmission of HIV infection and congenital syphilis. There is relative scarcity of information regarding the epidemiology of syphilis in India due to associated social discrimination; especially, with reference to uniform reporting from all parts of the country and comparison among various high and low risk groups. Knowledge about the trends of syphilis among the sexually transmitted diseases (STD) clinic patients, patients receiving anti-retroviral treatment (ART) and antenatal mothers may provide a better understanding of the disease. It may prove useful in the institution of effective preventive measures and management of syphilis cases.

Materials and Methods

This study extended over a period of six years from 2013-2018. It was carried out at the Immunology Laboratory, Microbiology Department of a tertiary care hospital in North India. All the serum samples that were sent for routine VDRL testing were included in the present study. No separate sample was collected for any purpose. The information regarding the age, gender and clinical department involved were recorded.

The samples received were segregated between the three groups-group one were the samples received from the sexually transmitted diseases clinic, group two were the samples received from the antiretroviral treatment clinic and the third group constituted of samples from the antenatal clinic. The sera was separated and stored at 4° C till further processing. All serum samples were screened by qualitative and quantitative VDRL test (Trepolipin kit of Tulip Diagnostics (P) Ltd., India) as per the manufacturer's instructions. VDRL test is a non-treponemal flocculation reaction which identifies the reaction between non treponemal antibodies and cardiolipin antigen. All the 762 samples reactive by VDRL testing over a period of six years (2013-2018) were recorded and analyzed to comparatively assess the trend of syphilis among the various high risk (STD and ART clinic attendees) and low risk (ANC clinic attendees) groups. The data analysis was performed using the Microsoft Excel sheet.

Results

A total of 77,634 serum samples were screened for syphilis by VDRL testing over a period of six years (2013-2018). Out of these, 762 samples were reactive. The trend of syphilis seroprevalence by VDRL testing over a period of six years is demonstrated in Figure 1 and Table 1. The overall seroprevalence of syphilis was 0.98% over the six years.

In the present study the age of the patients who tested reactive by VDRL ranged from being a neonate to 74

years old. Maximum number of VDRL reactive cases were seen in year 2018 followed by years 2017 and 2016 respectively (Figure 2, Table 2). Table 2 also shows the age wise distribution of syphilis cases in the years 2013-2018. 75.6% of these cases belonged to 18-35 years age group. Majority of the VDRL reactive cases belonged to 25-35 years age group followed by 18-25 years age group. 5.1% of the VDRL reactive cases were below 18 years of age. A male preponderance was seen among those tested reactive by VDRL in the present study with a male to female ratio of 1.1. The majority of the VDRL reactive males belonged to 25-35 years age group, whereas 18-25 years age group was the predominant age group among female patients.

The pattern of syphilis distribution among three groups over the past six years is shown in Figure 2. Patients attending the STD clinic are constantly the major contributor to VDRL reactive cases among the various departments followed by ART clinic attendees.

Figures 3, 4 and 5 depict the yearly trend of syphilis among STD, ART and ANC attendees respectively. Maximum number of VDRL reactive attendees from all the three study groups have been seen in the year 2018, followed by years 2017 and 2016.

Age wise distribution of syphilis among people attending STD, ART and antenatal clinics over the six years study period is shown in figures 6, 7 and 8 respectively. Among all the three groups majority of cases belonged to the 18-35 years age group.

The distribution of VDRL titers among the reactive cases in the STD, ART and ANC groups is shown in table 3 which also depicts the yearly trends in these titres. The low titers were most predominant in all the three VDRL reactive groups of STD, ART and antenatal clinic cases.

Discussion

The present study determined the current trend in the seroprevalence of syphilis by VDRL screening over a period of six years among the patients attending a tertiary care hospital. We have also assessed the yearly trend of syphilis among the various high risk (STD and ART clinic attendees) and low risk (ANC clinic attendees) groups. In the present study yearly seroprevalence of syphilis ranged from 0.33% to 2.19% with the highest seroprevalence in the year 2018. We have observed an increasing trend in the syphilis seroprevalence over successive six years with an exception of the year 2015 in which a fall was noted. However a suitable justification for the same could not be concluded. Our findings are in line with another study that has also reported a slow and gradual increase in syphilis seroprevalence during their study

Table 1: Syphilis seroprevalence by VDRL testing over a period of six years (2013-2018).

Year	Total samples tested	Total VDRL reactive samples	Syphilis seroprevalence(%)
2013	14744	48	0.33
2014	13041	70	0.54
2015	11708	43	0.37
2016	11697	123	1.05
2017	12728	177	1.39
2018	13716	301	2.19
Total	77634	762	0.98

Table 2: Age wise distribution of VDRL reactive cases in the years 2013-2018.

	2013	2014	2015	2016	2017	2018	Total (%)
<18 years							
Total	3	1	1	5	14	15	*39(5.1)
Male	2	0	1	1	5	5	**14(3.6)
Female	1	1	0	1	5	1	***9(2.5)
NA	0	0	0	3	4	9	*16 (2.1)
18-25 years							
Total	11	26	17	47	68	107	276(36.2)
Male	1	7	6	20	36	43	113(29.3)
Female	10	19	11	27	32	64	163(45.3)
25-35 years							
Total	23	29	16	41	65	125	299(39.2)
Male	9	8	12	23	39	64	155(40.2)
Female	14	21	4	18	26	61	144(40)
35-45 years							
Total	7	8	4	20	25	33	97(12.7)
Male	2	4	3	14	15	24	62(16.1)
Female	5	4	1	6	10	9	35(9.7)
45-55 years							
Total	3	4	4	8	3	12	34(4.5)
Male	2	3	0	7	2	12	26(6.7)
Female	1	1	4	1	1	0	8(2.2)
≥55 years							
Total	1	2	1	2	2	9	17(2.2)
Male	1	2	1	2	2	8	16(4.1)
Female	0	0	0	0	0	1	1(0.3)
Total VDRL reactive cases	48	70	43	123	177	301	762 (100)
Total number of VDRL reactive males	17	24	23	67	99	156	*386 (50.7)
Total number of VDRL reactive females	31	46	20	53	74	136	*360 (47.2)
Not available	0	0	0	3	4	9	*16 (2.1)

% calculated by considering the *total VDRL reactive cases, **total VDRL reactivemales, ***total VDRL reactive females as denominator respectively

Table 3: Distribution of various VDRL titers among VDRL reactive cases in the years 2013-2018.

VDRL Titre		2013	2014	2015	2016	2017	2018	Total (%)
R:1								
	Total (% out of total VDRL reactive cases in the same year)	21 (43.8)	31 (44.3)	16 (37.2)	12 (9.8)	31 (17.5)	62 (20.6)	*173(22.7)
	ART Clinic cases	13	9	2	3	10	23	**60(34.7)
	ANC cases	2	5	2	1	3	9	**22(12.7)
	STD clinic cases	6	17	12	7	17	18	**77(44.5)
	Others	0	0	0	1	1	12	**14(8.1)
R:2								
	Total(% out of total VDRL reactive cases in the same year)	13 (27.1)	10 (14.3)	8 (18.6)	20 (16.3)	35 (19.8)	65 (21.6)	*151(19.8)
	ART Clinic cases	2	3	5	4	13	24	**51(33.8)
	ANC cases	3	2	2	2	6	12	**27(17.9)
	STD clinic cases	8	5	1	11	14	21	**60(39.7)
	Others	0	0	0	3	2	8	**13(8.6)
R:4								
	Total(% out of total VDRL reactive cases in the same year)	4 (8.3)	7 (10.0)	5 (11.6)	22 (17.9)	26 (14.7)	48 (15.9)	*112 (14.7)
	ART Clinic cases	1	1	2	6	10	12	**32(28.6)
	ANC cases	1	0	0	4	1	7	**13(11.6)
	STD clinic cases	2	6	2	10	13	26	**59(52.7)
	Others	0	0	1	2	2	3	**8(7.1)
R:8								
	Total(% out of total VDRL reactive cases in the same year)	2 (4.2)	10 (14.3)	1 (2.3)	12 (9.8)	24 (13.6)	38 (12.6)	*87 (11.4)
	ART Clinic cases	0	6	0	4	12	9	**31(35.6)
	ANC cases	0	2	0	0	2	3	**7(8.0)
	STD clinic cases	2	2	1	7	9	26	**47(54.0)
	Others	0	0	0	1	1	0	**2(2.3)
R:16								
	Total(% out of total VDRL reactive cases in the same year)	2 (4.2)	3 (4.3)	5 (11.6)	19 (15.4)	16 (9.0)	25 (8.3)	*70(9.2)
	ART Clinic cases	2	0	0	5	10	6	**23(32.9)
	ANC cases	0	0	2	1	1	1	**5(7.1)
	STD clinic cases	0	3	3	12	5	17	**40(57.1)
	Others	0	0	0	1	0	1	**2(2.9)
R:≥32								
	Total(% out of total VDRL reactive cases in the same year)	6(12.5)	9(12.9)	8(18.6)	38(30.9)	45(25.4)	63(20.9)	*169(22.2)
	ART Clinic cases	2	5	5	9	18	25	**64(37.9)
	ANC cases	1	0	0	2	4	3	**10(5.9)
	STD clinic cases	3	4	3	25	20	31	**86(50.9)
	Others	0	0	0	2	3	4	**9(5.3)
Total cases		48	70	43	123	177	301	

% calculated by considering the *total VDRL reactive cases (762), **total VDRL reactive cases of that particular titer as denominator respectively

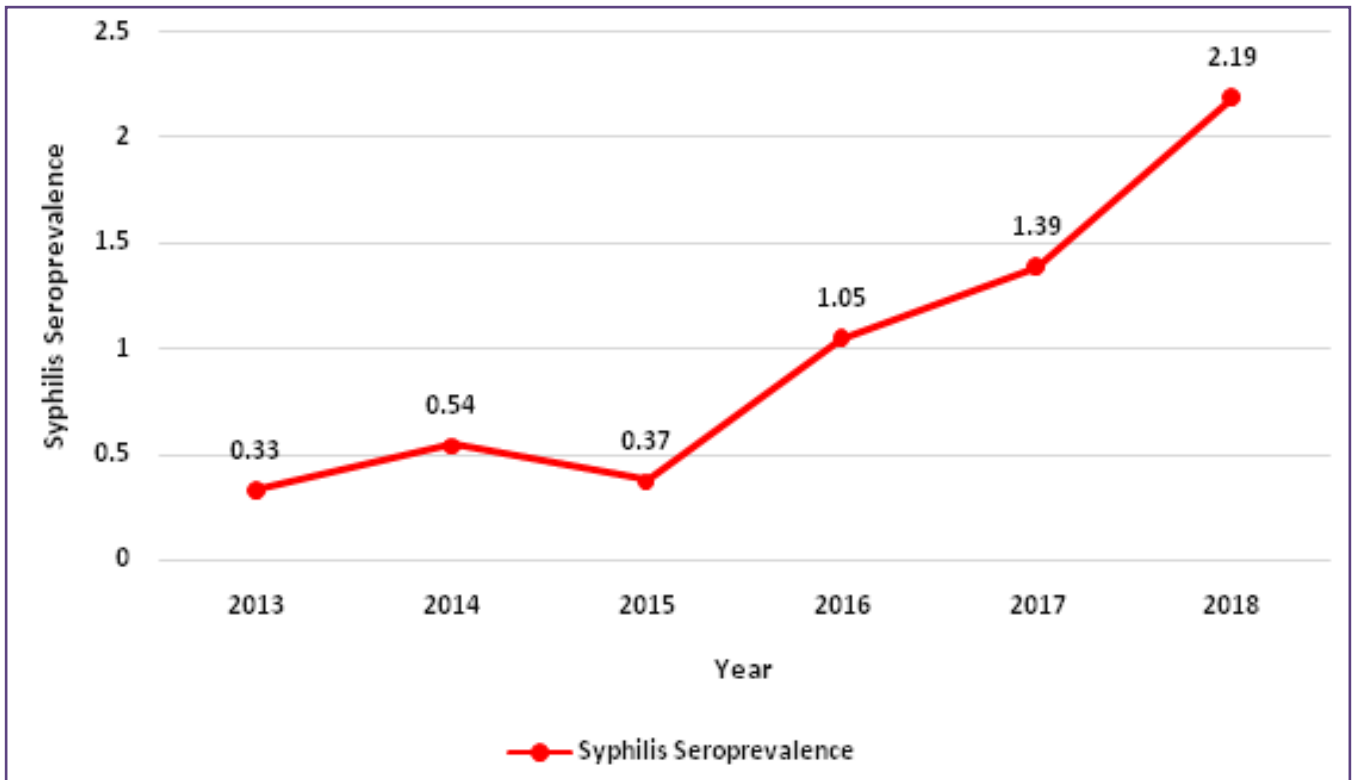


Fig. 1: Trend of syphilis seroprevalence by VDRL testing over a period of six years (2013-2018).

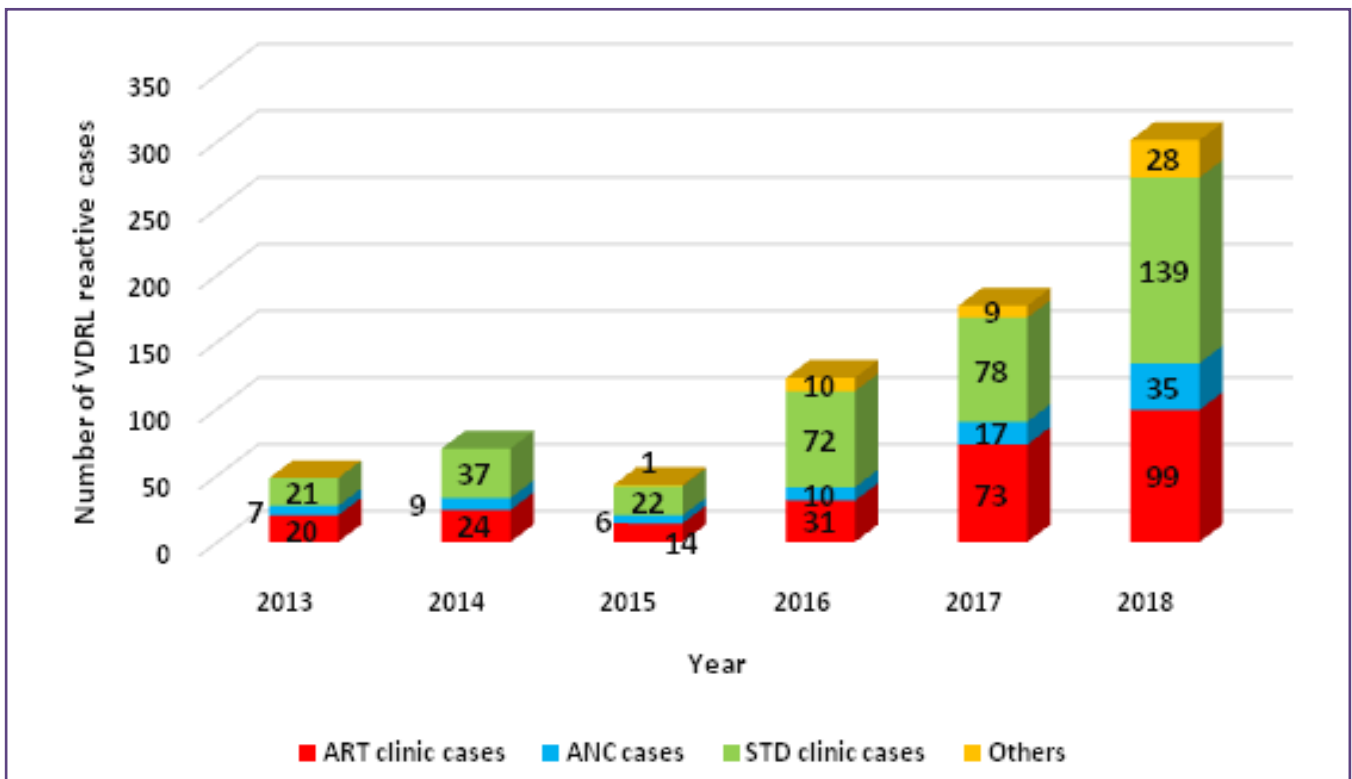


Fig. 2: Distribution of syphilis cases from year 2013-2018.

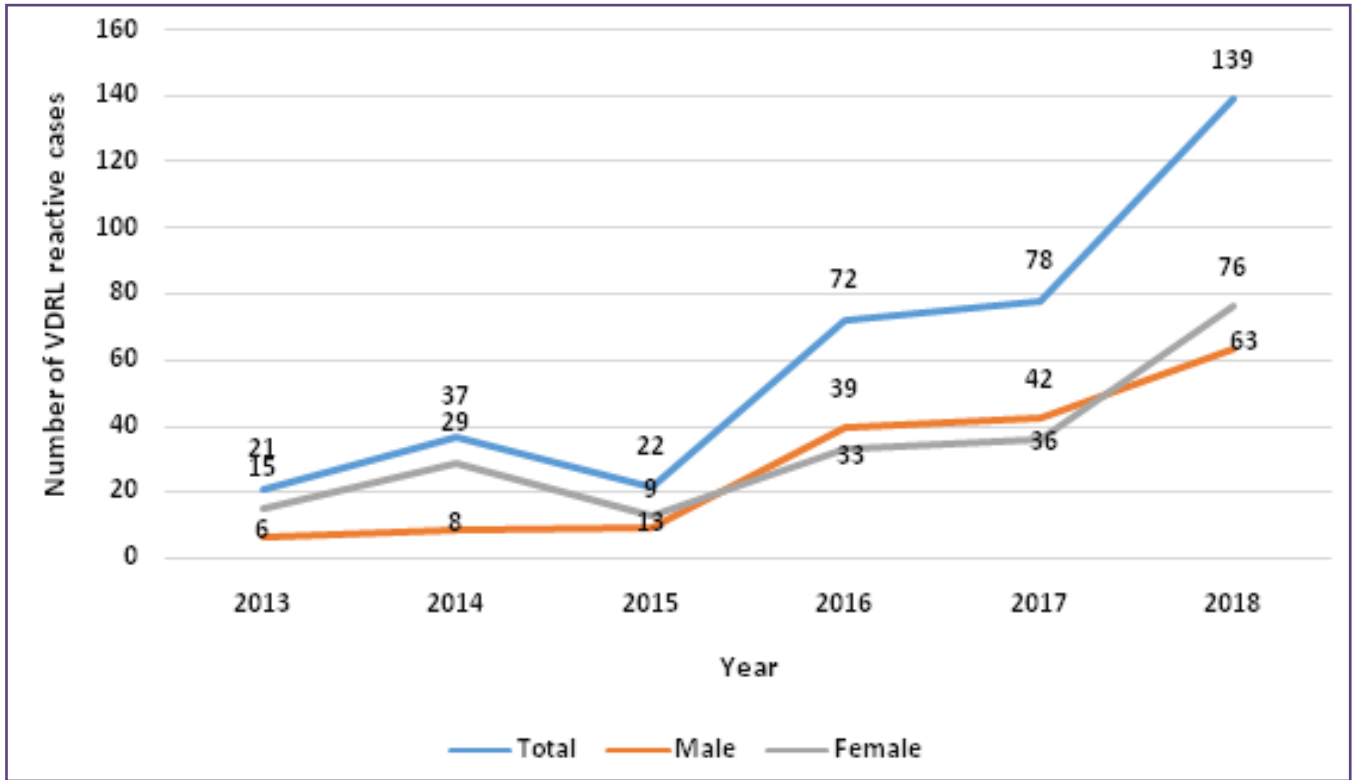


Fig. 3: Trend of syphilis among patients attending STD clinic from year 2013-2018.

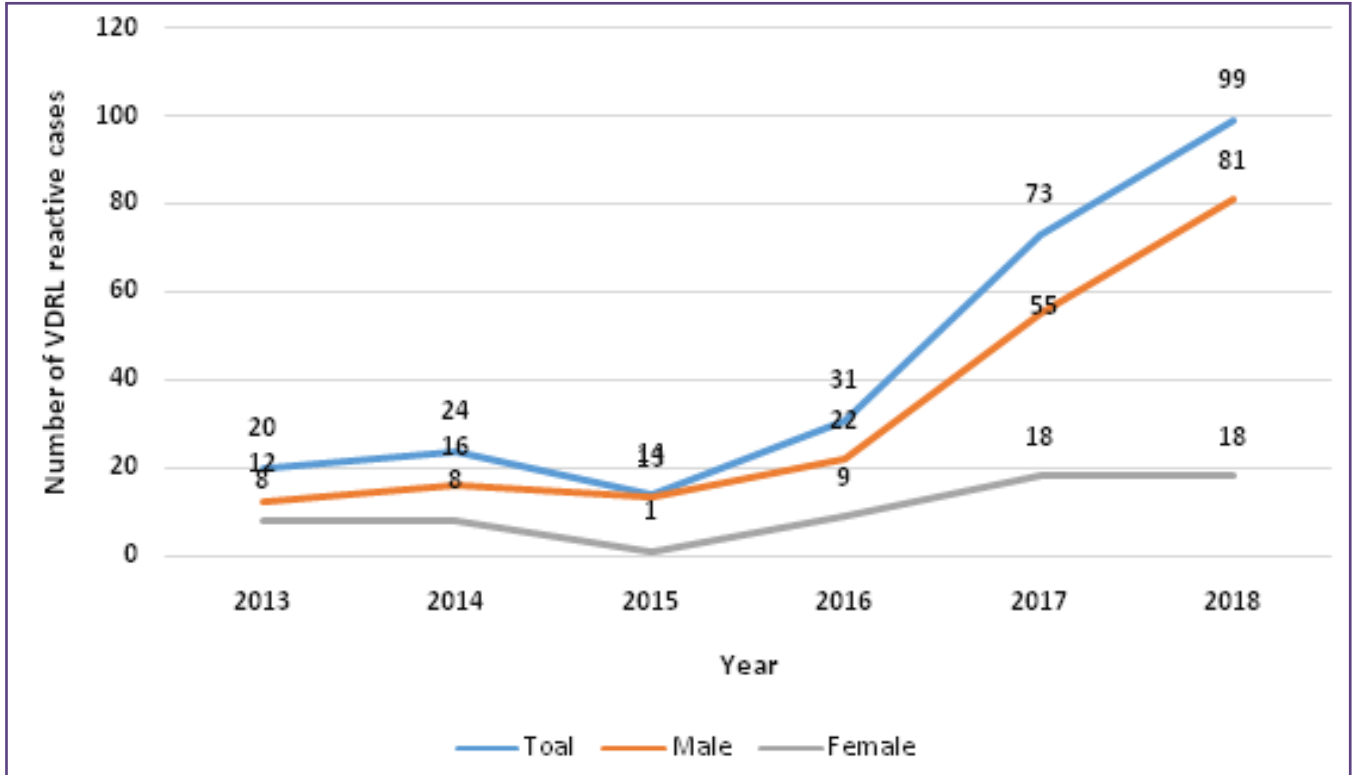


Fig. 4: Trend of syphilis among people attending ART clinic from year 2013-2018.

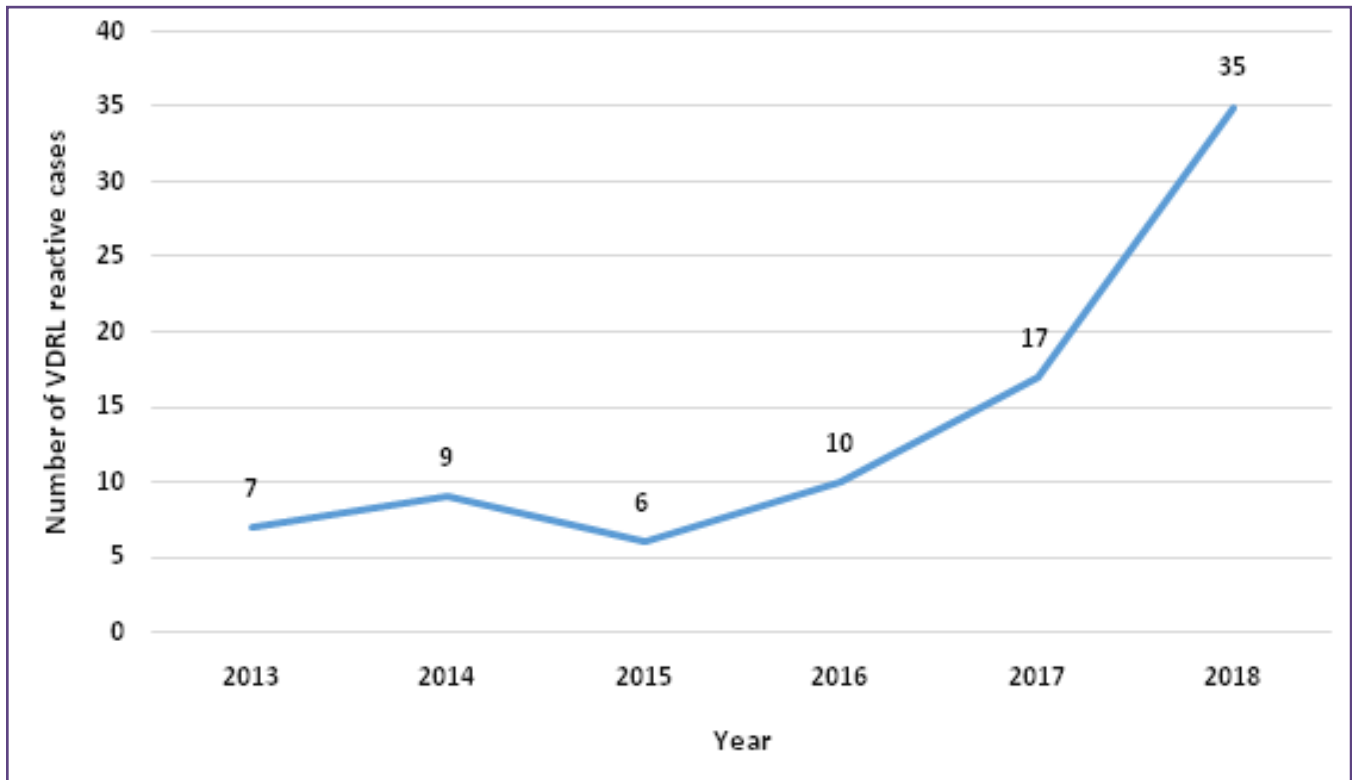


Fig. 5: Trend of syphilis among antenatal mothers from year 2013-2018.

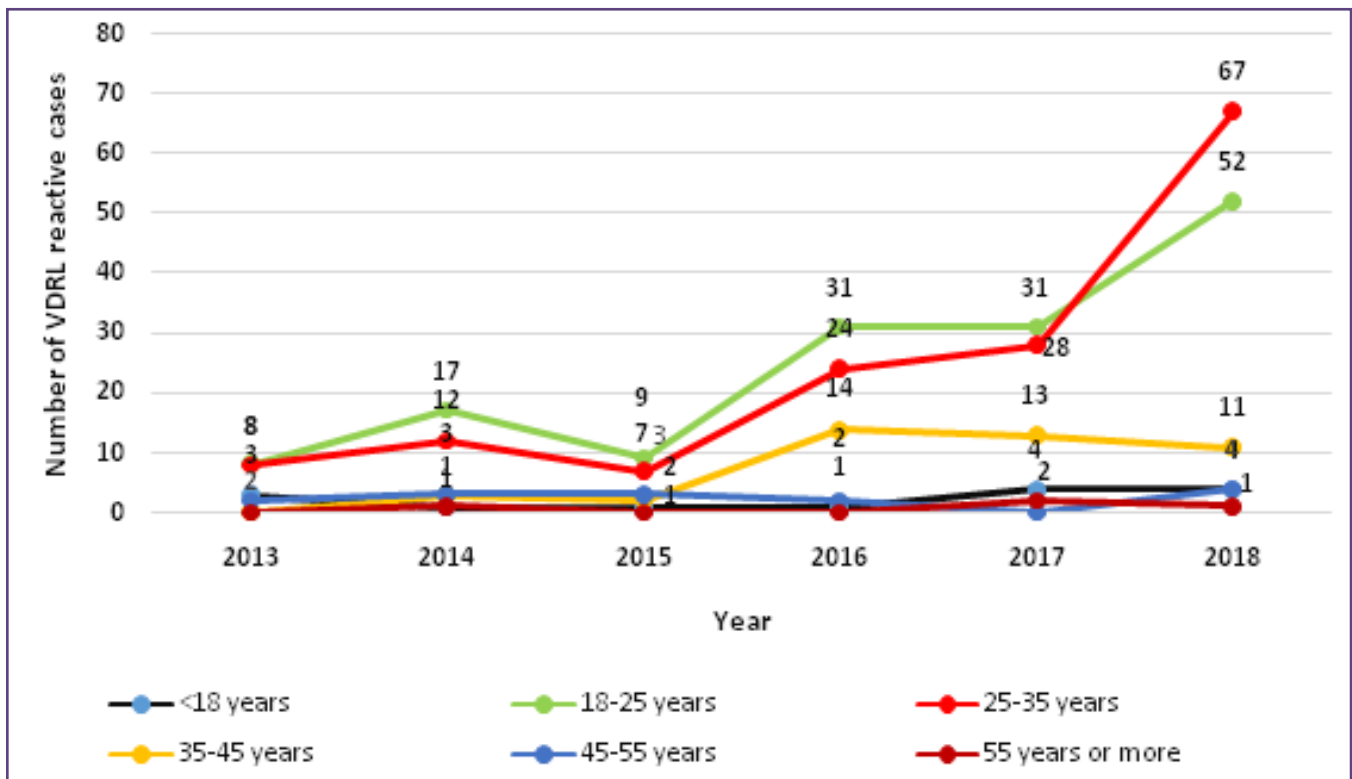


Fig. 6: Age wise distribution Of syphilis among people attending STD clinic from year 2013-2018.

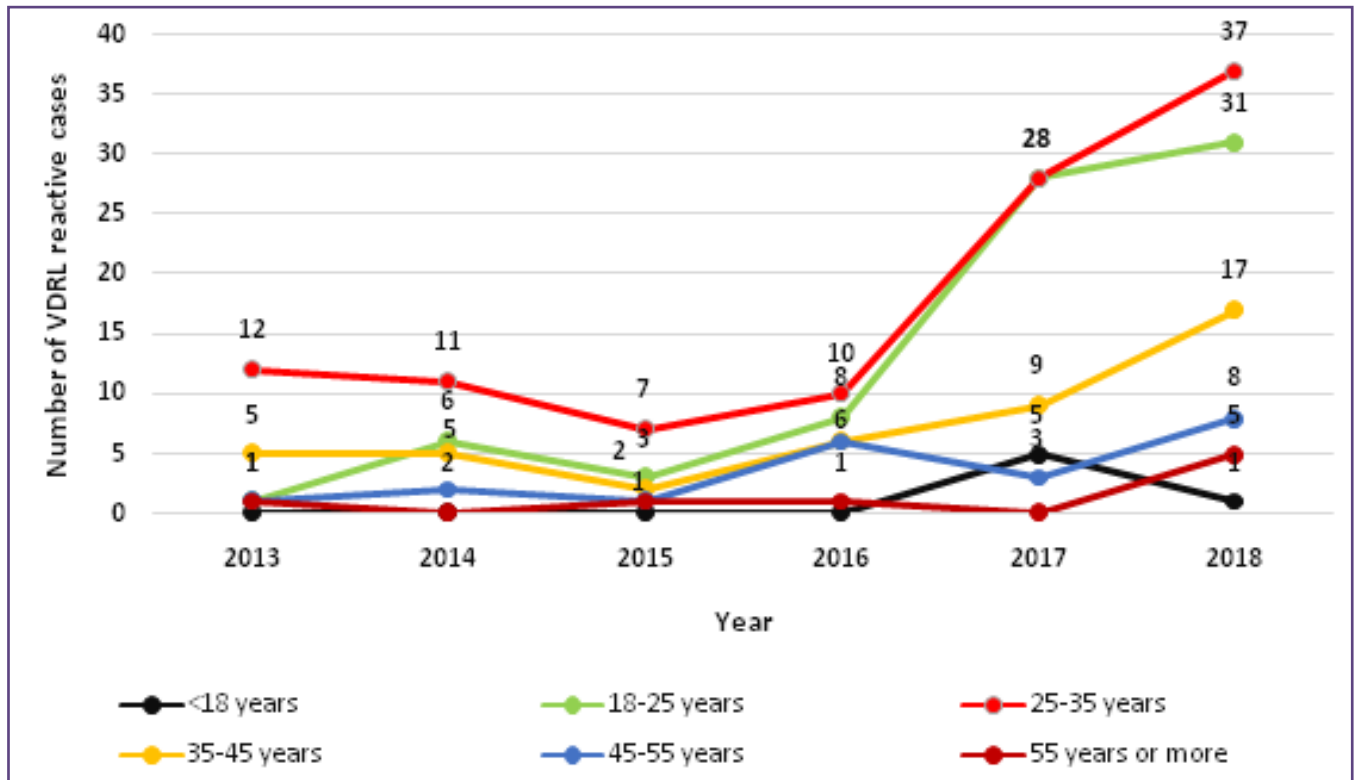


Fig. 7: Age wise distribution of syphilis among people attending ART clinic from year 2013-2018.

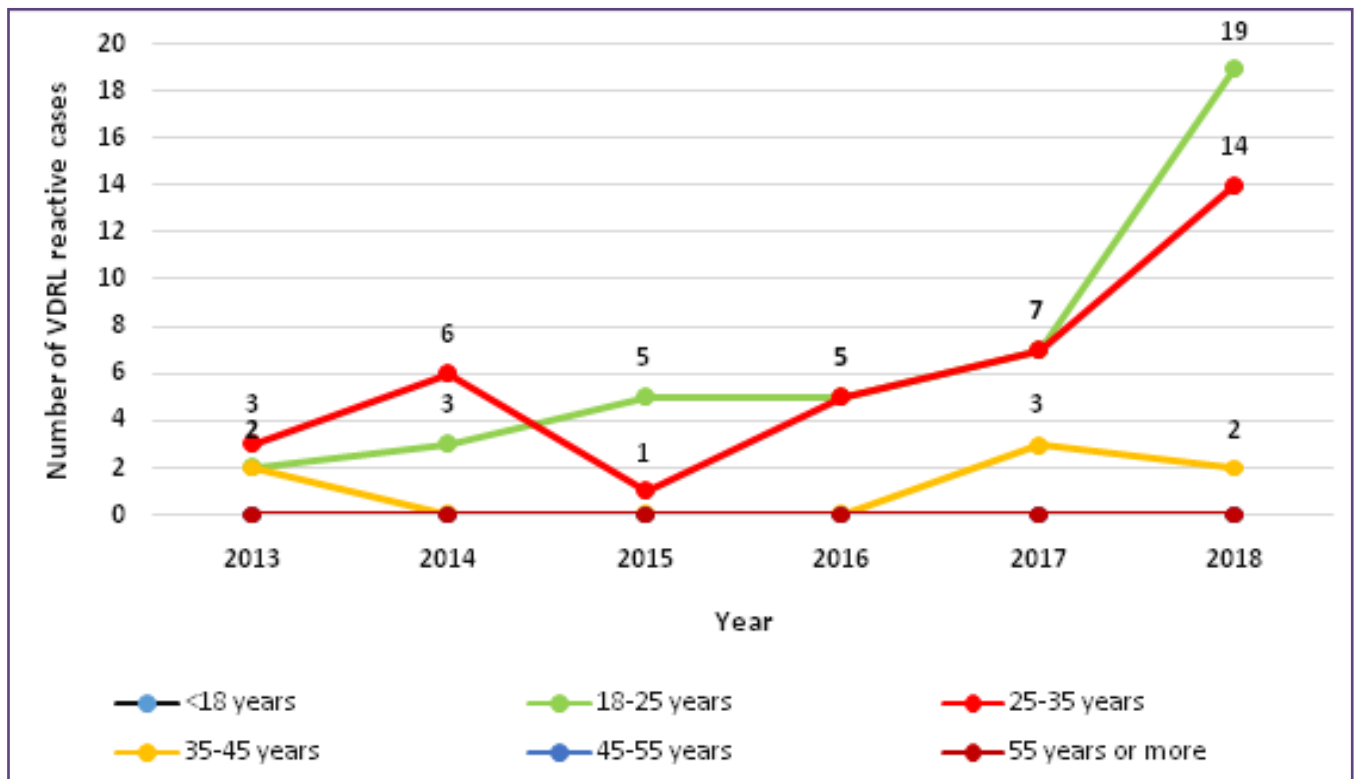


Fig. 8: Age wise distribution of syphilis among people attending ANC clinic from year 2013-2018.

duration (2006-2011).¹⁵ However another study reported no significant change in the trend of VDRL reactive cases over nine years.¹⁶ In our study we have reported an overall syphilis seroprevalence of 0.98% over the six years. A study from Southern India has documented a cumulative syphilis seroprevalence of 0.70% by VDRL testing.¹⁷ However Sethi S et al. have reported a higher total sero-reactivity of 3.36% samples by VDRL.¹⁵

In our study among all the age groups we observed the highest (39.2%) VDRL reactivity in 25-35 followed by 18-25 years age group. A previous report from the same laboratory has also documented the majority (59.69%) of the patients who tested positive (by at least one of the two tests, VDRL and TPHA) belonged to 15-30 years of age group.¹⁸ These are in line with the study by Sharma A et al. that has also reported maximum VDRL positivity in the age group of 21-30 years age group each year.¹⁶ In the last four years (2015-2018), we have observed an upward trend in the VDRL reactive cases in the 18-45 years age groups. Our study further suggests an increasing trend of VDRL reactivity in below 18 years age group. These findings may point towards the increasing practices of unsafe sexual behaviour and inadequate awareness towards the same in the population. Another study has observed a decreasing trend of VDRL sero-positivity in 10-20 years age group.¹⁶

In the present study we have noted a male preponderance among VDRL reactive cases amounting to 50.7% of the total VDRL reactive cases. Our findings are in agreement with another study reporting 51.83% of total patients testing positive (by at least one of the two tests, VDRL and TPHA) as males.¹⁸ The greater involvement of males in outdoor activities among our patient strata could probably account for that. Sethi S et al. have also reported more males to be positive as compared to females.¹⁵ Though we observed an increasing trend of VDRL reactivity among both the sexes in our study. Another study, however, reported an increasing trend of VDRL positivity among men while the same was declining among women.¹⁶

Syphilis is probably the predominant STD in India. ¹⁹In the present study majority of the VDRL reactive cases were the STD clinic attendees in each year. Our findings are in agreement with the previous study in which the STD clinic cases formed the majority among those tested positive by at least one of the tests of VDRL or TPHA.¹⁸ Our study has reported a rise in the number of VDRL reactive STD clinic attendees in each successive year for the past three years. Sharma A et al. in their study have reported not much change in the VDRL positivity among STD clinic attendees.¹⁶ The failure in achieving the decline in syphilis

cases further emphasises the need of upscaling the efforts for the effective control of syphilis.

The present study has demonstrated an overall upward trend of VDRL reactivity among the ART clinic attendees over last six years. The majority of these cases belonged to 18-45 years age group. Unfortunately the diseases of syphilis and HIV affect the economically productive age group, thus affecting a wider population than the ones actually involved besides the risk involved in the transmission of the disease to the partners. Sexual transmission is the most common mode of transmission for syphilis and HIV. Ulceration and inflammation involved with STDs can enhance the risk of transmission of HIV infection.

Antenatal mothers contributed the least number of VDRL reactive cases among the three study groups in each year. Our findings are in agreement with the previous study which also reported the highest cases of probable active syphilis infection from STD clinic attendees followed by ART and antenatal clinic attendees.¹⁸ Overall the number of VDRL reactive antenatal mothers has shown a rising trend over the past years in our study. However, another study reported a gradual decline in VDRL positivity in the antenatal clinic attendees.¹⁶ Partner notification and contact tracing become integral components in the prevention and management of any STD.

The epidemiology of syphilis and HIV infections has been reported to alter over time periods with various study populations and geographic areas.^{20,21} In our study too if we compare the increase in positive cases among the total samples tested from 2013 to 2018, the steepest rise is seen with the STD group while the ANC remains the lowest. Our study provides a better understanding of the current trend of syphilis among the ART, STD and ANC clinic attendees. This may prove to be very useful in the development of protocol for the better prevention and control of syphilis infection.

Conclusion

Despite the several ongoing campaigns highlighting the importance of safe sexual practices, public awareness activities about HIV and other STDs, adoption of syndromic approach for the management of STDs and antenatal screening, the number of syphilis cases are constantly increasing in our community. It is crucial to understand the current trend and epidemiology of syphilis among ART, STD and ANC clinic attendees for the proper planning and implementation of preventive and control strategies separately targeted at the various high and low risk groups. Only a better understanding of the patterns of syphilis can aid us in making a progress towards controlling this public health issue.

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*Corresponding author:

Dr. Bineeta Kashyap, Flat no. C-402, Vimal CGHS LTD., Plot-3, Sector-12, Dwarka, New Delhi-78

Phone: +91 9899583514

Email: dr_bineetakashyap@yahoo.co.in

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