Original Article

A 10 year Retrospective Study on HIV-2 : A Neglected Cousin of HIV-1

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ABSTRACT

Background: Though HIV-2 has slower rates of progression to AIDS and death, differentiating it from HIV-1, is important as choice of ART (antiretroviral therapy) is different.

Aims and Objectives: To study the prevalence of HIV-2 infection at Mahathma Gandhi Memorial Hospital, Warangal and to study the age, gender, occupation and behavior of the HIV-2 infected persons.

Materials and Methods: A retrospective study of 10 years was carried out from January 2008 to December 2017 in persons attending Integrated counselling and testing centre (ICTC) at Mahathma Gandhi Memorial Hospital, Warangal. They were screened by WHO strategy III of HIV testing. HIV reactive sera by COMBAIDS (enzyme immunoassay) were further tested by MERISCREEN-WB (immunochromatographic assay) and AIDSCAN (flow through immunodottest). HIV 1 and 2 co-infected sera, HIV -2 reactive sera and indeterminate cases were confirmed by western blot test from National reference laboratory.

Results: Comparison between HIV-1, HIV-2, HIV 1 & 2 positive groups for age, gender, route of transmission was made using chi-square test. P value<0.05 was considered as significant. Of the total 61,741 serum samples tested, 8397 (13.60%) were positive for HIV antibodies. Out of the reactive sera 97.86%, 1.14%, 1.00% were reactive for HIV-1, HIV-2, HIV1 and 2 respectively. Among reactive sera, prevalence of HIV-2 was 2.14%.

Conclusion: Though HIV -1 epidemic is progressing faster than that of HIV-2, monitoring of HIV-2 epidemic is essential to determine the extent of problem in India. HIV reactive sera must be differentiated in two types of HIV infection as HIV-2 treatment regimen is different from HIV -1, or else we have to face serious resistant strains of HIV-2.

Keywords: Prevalence, HIV-2, ICTC

INTRODUCTION

Human immunodeficiency virus type-2 (HIV-2) belongs to the family Retroviridae. It was in 1985 that researchers found evidence for this second species of human immunodeficiency virus (HIV) among commercial sex workers (CSW) in Senegal (West Africa). [1]

This virus is morphologically similar to human immunodeficiency virus type1 (HIV-1) but has got only a 40% homology at the nucleotide level. [2] HIV-2 epidemic has its epicenter in West Africa, and is also found in those countries that have had historical colonial links with the region, in particular Portugal and France. It has also been reported infrequently in parts of India with previous ties to Portugal.[3] The first report of HIV-2 in India was from the port city of Mumbai in 1991 and soon after infected individuals were identified from south Indian port cities of Chennai and Visakhapatnam. [4]

HIV-2 is associated with lower viral load levels and slower rates of CD4 decline and clinical progression compared with HIV-1.[5,6] The transmission rate for HIV-2 compared to HIV-1 is very low both by heterosexual route and mother to child transmission.

The clinical signs and symptoms of immunodeficiency associated with HIV-2 are similar to the ones seen among

the HIV-1 infected individuals and they can also progress to AIDS. [2] However, there was no observed difference in the mortality rate among the HIV-1, HIV-2 and dually infected individuals with < 200 CD4 cells although a significant lower mortality was observed among HIV-2-infected individuals with CD4 count of > 500 cells/µl. [7, 8]

The choice of antiretroviral therapy for HIV-2 differs from that for HIV-1, as HIV-2 has intrinsic resistance to the 'first-generation' non-nucleoside reverse transcriptase inhibitors (NNRTIs), nevirapine and efavirenz.

HIV-2 strains infected individuals also show mutations due to presence of several natural polymorphisms in the protease gene. [9, 10, 11] This underscores the importance of differentiating HIV types.

Our current study was planned to find out prevalence of HIV-2 infection at Integrated counselling and testing centre (ICTC) at Mahatma Gandhi Memorial Hospital , Warangal over a period of 10 years (January 2008 to December 2017) and also to study the age, gender, route of transmission of HIV-2 infected persons.

MATERIALS AND METHODS

A total of 61,741 serum samples were collected between January 2008 to December 2017 from persons attending the Integrated counselling and testing centre (ICTC) at Mahatma Gandhi Memorial Hospital and screened by WHO strategy III of HIV testing, after pretest counseling.

Reactive sera by COMBAIDS (enzyme immunoassay) were further tested by MERISCREEN-WB (immuno chromatographic assay) and AIDSCAN (flow through immunodottest which can differentiate HIV1 and 2.

The tests were performed and interpreted as per manufacturer's instructions. HIV 1 and 2 co-infectedsera, HIV-2 reactive sera and indeterminate cases were sent to National reference laboratory for confirmation by western blot.

STATISTICAL ANALYSIS

Comparison between HIV-1, HIV-2, HIV 1 & 2 positive groups for age, gender, route of transmission was made using chi-square test. p value < 0.05 was considered as significant.

RESULTS

Of the total 61,741 serum samples tested, 8397 (13.60%) were positive for HIV antibodies. Out of the reactive sera (n=8217) 97.86%, (n=96) 1.14%, (n=84)1.00% were HIV-1only, HIV-2 only, HIV 1 and 2 respectively. There were

Table1: Showing seroprevalence of HIV types in 10 years (January 2008 to December 2017)

Year	Tested (n=61,741)	Reactive (n=8397)	%	HIV-1 only (n=8217)	%	HIV-2 only (n=96)	%	HIV 1&2 (n=84)	%
2008	4874	1288	26.42	1271	26.07	8	0.17	9	0.18
2009	5530	1204	21.77	1189	21.50	7	0.13	8	0.14
2010	5965	1116	18.70	1098	18.41	13	0.21	5	0.08
2011	4876	1097	22.49	1070	21.94	16	0.32	11	0.22
2012	5402	900	16.66	873	16.16	4	0.07	23	0.61
2013	6494	639	9.83	628	9.67	5	0.07	6	0.09
2014	7450	610	8.18	598	8.02	7	0.09	5	0.07
2015	7765	514	6.61	496	6.38	9	0.11	9	0.11
2016	6921	533	7.70	510	7.37	17	0.24	6	0.09
2017	6464	496	7.67	484	7.49	10	0.15	2	0.03

Table 2: Sex-wise distribution of HIV reactive sera

Year	HIV 1				HIV 2				HIV 1 & 2			
	Male (n=4597)	Female (n=3506)	TG (n=114)	Total (n=8217)	Male (n=52)	Female (n=44)	TG	Total (n=96)	Male (n=52)	Female (n=31)	TG (n=1)	Total (n=84)
2008		553	3	1271	5	3	-	8	6	3	-	9
2009		487	27	1189	4	3	-	7	7	1	-	8
2010		481	4	1098	8	5	-	13	5	-	-	5
2011		440	11	1070	10	6	-	16	6	5	-	11
2012		359	14	873	2	2	-	4	12	11	-	23
2013		281	14	628	3	2	-	5	2	3	1	6
2014		254	26	598	2	5	-	7	4	1	-	5
2015		200	11	496	5	4	-	9	5	4	-	9
2016		227	2	510	8	9	-	17	3	3	-	6
2017		224	2	484	5	5	-	10	2	-	-	2

Table 3: Age- wise distribution of reactive sera

Year	HIV 1 (n= 8217)					HIV 2 (n=96)					HIV 1&2 (n=84)				
	0-14	15-24	25-34	35-49	>50	0-14	15-24	25-34	35-49		0-14	15-24	25-34	35-49	>50
2008	62	165	438	466	140	-	-	1	7	-	-	2	1	5	1
2009	47	157	421	451	113	-	-	2	4	1	-	-	4	4	-
2010	29	118	407	434	110	-	-	5	7	1	-	-	-	5	-
2011	24	115	378	415	138	-	-	3	9	4	1	-	1	7	2
2012	17	116	250	370	120	-	-	-	2	2	1	-	11	8	3
2013	19	59	165	268	117	-	-	2	2	1	-	-	1	4	1
2014	19	87	152	248	92	-	-	-	4	3	-	-	-	3	2
2015	10	36	153	220	77	-	-	-	7	2	-	-	2	7	-
2016	14	40	124	235	97	1	-	-	11	5	-	1	1	3	1
2017	12	44	106	221	101	-	-	1	4	5	-	-	-	2	-
TOTAL	253	937	2594	3328	1105	1	-	14	57	24	2	3	21	48	10

Table 4: Characteristics of individuals with HIV reactive sera

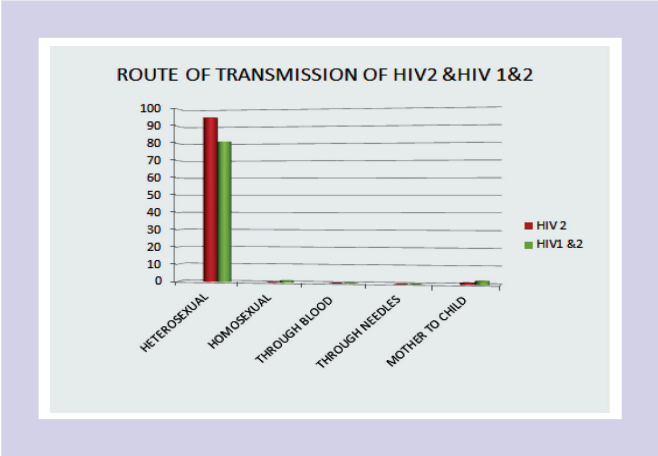
Variable	HIV I n (%)	HIV 2 n (%)	HIV 1&2 n (%)	Total
Total n=	8217 (97.86%)	96 (1.14%)	84 (1.00%)	8397(13.60%)
Age (Years)				
0-14	253 (98.83)	1 (0.39)	2(0.78)	256 (3.05)
15-24	937 (99.69)	-	3 (0.31%)	940 (11.20)
25-34	2594 (98.67)	14 (0.53)	21(0.80)	2629 (31.30)
35-49	3328 (96.94)	57 (1.66)	48 (1.40)	3433 (40.90)
>50	1105 (97.00)	24 (2.10)	10 (0.90)	1139 (13.55)
Sex				
Males	4597 (97.8)	52 (1.10)	52 (1.10)	4701(55.98)
Females	3506 (97.90)	44 (1.23)	31 (0.87)	3581 (42.65)
Transgender (TG)	114 (99.13)	-	1 (0.87)	115 (1.37)
Route of Transmission				
Heterosexual	6935 (97.53)	95 (1.33)	81 (1.14)	7111
Homosexual	261 (99.62)	-	1 (0.38)	262
Through blood & Blood products	4	-	-	4
Through infected Syringes, needles	2	-	-	2
Mother to child	311 (99.04)	1 (0.32)	2 (0.64)	314
Type of Positive Cases				
Female sex workers	91 (63.2)	29 (20.13)	24 (16.67)	144
MSM	246 (99.60)	-	1 (0.40)	247
Injecting drug users	4	-	-	4
Truckers	30 (61.22)	7 (14.29)	12 (24.49)	49
With STDs	197 (79.76)	32 (12.96)	18 (7.28)	247
Migrants	52 (82.53)	4 (6.35)	7 (11.12)	63
Antenatal cases	5	-	-	5

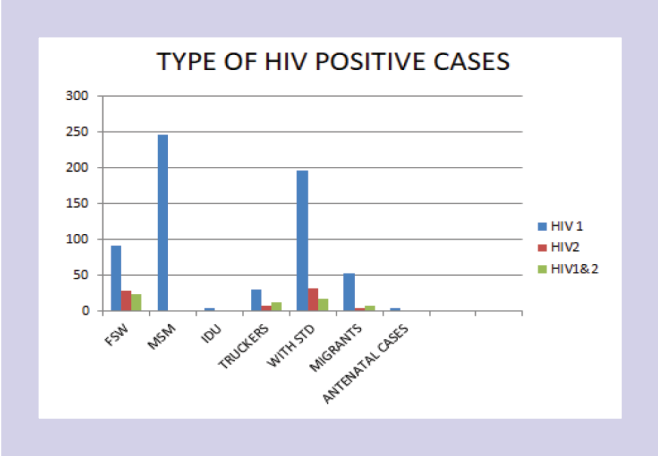
no indeterminate cases after testing with western blot at National reference laboratory.

Among reactive cases, seroprevalence ofHIV-2 was 2.14%.There is a decline in the prevalence of HIV-1, HIV-2, HIV 1& 2 types over a period of 10 years.

Over all , HIV types were statistically significant among males (p=0.0001), predominant in 35-49 years age group.

Most common route of transmission of HIV-2 was heterosexual (1.33%) and mother to child transmission



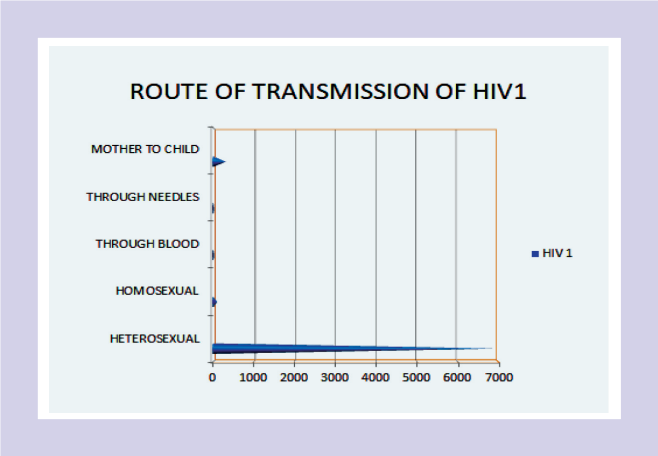


of HIV-2 was 1(0.32%) noted. HIV 1 and 2 co-infected sera were 81(1.14%) among heterosexuals, 1 (0.38%) among homosexuals, 2 (0.64%) children were affected due to mother to child transmission. Highest prevalence of HIV-2 was seen among persons with high risk behaviour.

DISCUSSION

HIV-2 is much less common compared to HIV-1, has to be confirmed by HIV-2 Western Blot test. Both HIV-1 and HIV-2 have the same modes of transmission, but HIV-2 is said to be less infectious and mother-to-child transmission is rare. The clinical course of HIV-2 infection is slower, plasma HIV-2 RNA levels are lower as compared to HIV-1 infection, but once the illness progresses to AIDS, the course is similar to HIV-1. [12]

In geographical regions where a dual epidemic of HIV-1 and HIV-2 is ongoing, the serological reactivity to both the viruses in an infected individual may be a source of diagnostic difficulties. [13] The dual sero-reactivity may be due to one of the following reasons (a) a mixed infection (b) broad immune response against infection with a single strain of HIV-1 or HIV-2 (c) infection with a unique third virus containing epitopes common to either viruses or (d) exposure to both viruses but established



infection with only one. [14]

In co-infected cases the course of the illness is like in HIV-1, however, one has to give the therapy as we would in isolated HIV-2 infection. Reliable viral load measurement is not yet possible for HIV-2 infection; hence the patient's response has to be judged clinically and by CD4 counts. [15]

In India, HIV-2 kits were made available under the national AIDS control program in 2012. HIV-2 is intrinsically resistant to nonnucleoside reverse transcriptase (NNRTI) drugs, Nevirapine and Efavirenz.

The options available for firstline HIV-2 treatment are the second line drugs for HIV-1 i.e. Nucleoside reverse transcriptase inhibitors, NRTIs- zidovudine, lamivudine, tenofovir or abacavir or boosted protease inhibitors (PI-based) regimes, using saquinavir, lopinavir, darunavir, or indinavir. Boosted PI regime has been suggested by the U.S. department of Health and Human services. [16]

Drugs used in Government ART centres in India under the umbrella of NACO are Tenofovir 300mg + Lamivudine 300 mg + Lopinavir 200 mg + Ritonavir 50 mg. It is observed that there is a significant rise in CD4 count and weight gain, after initiation of second line ART as per NACO guidelines in cases of HIV-2 positive patients after at least one year of therapy. [12]

There is a decline in seroprevalence of HIV types in the present study indicating that early diagnosis and treatment of the disease, also increasing awareness, knowledge about the transmission of HIV would further reduce the prevalence of this disease.

In India, predominant mode of transmission of HIV-2 is heterosexual route. Mother to child transmission was seen in studies conducted by Murugan S et al inTamilnadu [17] 2(11.11%), children affected out of 18 HIV-2 patients, Agarwal S et al in Mumbai [8] 3 (2.01%) children affected out of 149 HIV-2 patients, Nayana AI et al in Mumbai [9]

1(1.04%) out of 96 HIV-2 patients.

In the present study in Warangal (Telangana) 3(1.67%) reactive cases were found out of 180 HIV-2 patients.

All infants born to mothers with HIV-2 should receive a 6-week zidovudine prophylaxis regimen. [11, 18] The rationale for zidovudine prophylaxis in this clinical situation is based on the inability to monitor HIV-2 plasma viral load in the mother and the lack of nevirapine activity against HIV-2, which precludes its use as prophylaxis. [18, 19]

CONCLUSION

HIV reactive sera must be differentiated into types of HIV infection. There is a need to introduce viral load assays for monitoring HIV-2 and also new prophylactic measures in preventing mother to child transmission of HIV-2 or else we have to face serious resistant strains of HIV-2.

CONFLICT OF INTEREST:

The authors declared no conflict of interest

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