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Original Article
Prevalence of HIV-2 infection in a tertiary care centre in Akola, Maharashtra

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ABSTRACT

Introduction: In world HIV-2 virus was first isolated in West Africa in 1986 and is mainly restricted to West Africa. Due to increase in population mobility HIV-2 has spread from West Africa to other parts of world. In India HIV-2 cases are comparatively less and having geographically diverse spread in various states. HIV-2 infection is generally characterized by a longer asymptomatic stage, lower plasma viral loads, and lower mortality rate than HIV-1 infection. Aims & Objective: This study was conducted to determine the seroprevalence of HIV-2 and dual infection in HIV-infected individuals at the tertiary care center in Maharashtra. Materials and Methods: All the samples submitted for HIV testing at ICTC in GMC Akola during 5 years study period were included in the study. Following NACO guidelines, after informed consent and pre-test counseling patient's blood sample were tested for HIV using testing strategy III (7). The samples positive for HIV-2 or dual infection were sent to NARI, Pune for further testing and confirmation. Observations & Results Out of 67969 patient's samples tested for HIV 1.97% (n=1341) were positive for HIV antibodies. Out of 1341 patients 58.9% were male and 41.1% were female patients. Out of total samples tested 1.95% (n=1329) samples were HIV-1 positive, 0.014 % (n=10) were HIV-2 positive and 0.0029 % (n=2) were positive for both HIV-1 and HIV-2 (dual infection). Compared with HIV-1, HIV-2 positive patients represent very small proportion of all diagnosed HIV patients. Out of 1341 positive patients 58.9% (790) were male patients and 41.1% ((551)) were female patients. From all HIV-2 positive patients 50% patients were in age group of 31-40 years. Conclusion: In present study we conclude that the incidence of HIV-2 and dual infection does occur in Akola but it is comparatively less prevalent than other parts of India. As HIV-2 may pose serious threat in future, enhancing the diagnosis by detecting HIV-2 by various methods and correct treatment of HIV-2 infection according to new guidelines is the need of time for India.

1. Introduction

Human immunodeficiency virus (HIV) is the etiological agent of Acquired Immunodeficiency Syndrome (AIDS) and it has rapidly spread around the world affecting nearly 37.9 million people worldwide at the end of 2018[1]. India has an approximately 21 lakhs People Living with HIV (PLHIV) in 2017[2]. HIV is a retrovirus having 2 serotypes, HIV-1 and HIV-2. HIV-2 is more similar to Simian immunodeficiency virus (SIV) and having 40% genetic identity with HIV-1. HIV infection is divided into HIV-1infection only, HIV-2 infection only or HIV-1 and HIV-2 (dual) infection. Majority of cases detected are of HIV-1 type and small number of cases are of HIV-2 or dual infection seen. In world HIV-2 virus was first isolated in West Africa in 1986 and in India first case was reported in Mumbai in 1991[3]. HIV-1 infection has spread globally all over the world but HIV-2 is ter mainly restricted to West Africa. Due to increase in population mobility HIV-2 has spread from West Africa to other parts of world. In India HIV-2 cases are comparatively less and having geographically diverse spread in various states. Globally, it has been estimated that one million to two million individuals have HIV-2[4]. Currently exact data of HIV-2 infection is not available in India. At present in majority of testing centers diagnosis of HIV-2 is done by rapid tests following NACO guidelines and sample will be sent to higher center for confirmation by more specific tests like Western blot test or nucleic acid test.

HIV-2 infection is generally characterized by a longer asymptomatic stage, lower plasma viral loads, and lower mortality rate than HIV-1 infection[5]. HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors and to Enfuvirtide; therefore, redesigning the antiretroviral therapy (ART) regimens for effective control over progression of disease to AIDS should be done for HIV-2 infection [6]. The monitoring of HIV-2 patient should be done by periodic CD4 cell count testing even if their viral loads are persistently suppressed, because disease progression

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can occur despite an undetectable viral load. Considering above facts about HIV-2 this study was conducted to determine the seroprevalence of HIV-2 and dual infection in HIV-infected individuals at the tertiary care center in Akola.

Objectives:

The objective of this study is to determine the seroprevalence of HIV-2 and dual infection in HIV-infected individuals at our cenMaterials and Methods :

This prospective study was conducted at a tertiary care teaching hospital in Government Medical College, Akola from 1 January 2014 to 31 December 2018 was conducted after approval from the Institutional Ethics Committee. All the samples submitted for HIV testing at integrated counseling and testing center (ICTC) in GMC Akola during study period were included in the study. Following the guidelines of the National AIDS Control Organization (NACO), after informed consent and pre-test counseling patient's blood sample were tested for HIV using testing strategy III [7]. First test performed was rapid comb test (Comb Aids, ARKARY health Pvt.ltd.) following manufacturer's instructions. If the test was non-reactive then further testing was not done and patient reported as negative for HIV antibodies. If first test was reactive for HIV then two more rapid tests were carried out on the same sample. The second test performed was immunofiltration test (Trispot MERISCREEN, Meril diagnostic Pvt.Ltd). The third test performed was immunochromatography test (Signal HIV, ARKRAY health Pvt.ltd). second and third tests were able to differentiate between HIV-1 and 2. After performing all 3 tests samples were reported as reactive for HIV-1 or HIV-2 or HIV-1& HIV-2 dual infection. The diagnosis of HIV-1 or HIV-2 or dual infection is based mainly on the rapid tests used. If the sample was positive for HIV-2 or dual infection then the that sample was sent to National AIDS Research Institute (NARI) Pune for further testing and confirmation. All patients of all age group newly diagnosed with HIV or known cases who came to ICTC for HIV testing during study period were included, after obtaining informed consent.

The discrete data is mentioned in the form of numbers and percentages. 2 proportion test is used to calculate the P value between the groups. The P value of <0.05 is considered as statistically significant. The data is analyzed by SPSS software version 18.

Results :

Table 1 shows yearly data of total samples collected and screened for HIV infection during study period at ICTC, GMC Akola. During study period a total of 67969 samples were tested for HIV antibodies. From those 67969 samples 35905 were males and 32064 were females. Out of total 67969 samples 1.97% (n=1341) samples were positive for HIV antibodies among which 1.95% (n=1329) samples were HIV-1 positive, 0.014 % (n=10) were HIV-2 positive and 0.0029 % (n=2) were positive for both HIV-1 and HIV-2 (dual infection). With dual infection included, the overall HIV-2 prevalence was 0.016%. Compared with HIV-1, HIV-2 positive and dual infection patients represent very small proportion of all diagnosed HIV patients [0.90% (12) HIV-2 patients Vs 99.1% (1239) HIV-1 patients]. It was observed that over the period of 5 years the number of samples tested increased by 92% and prevalence of HIV positive decreased by 62%.

Table 2 contains the agewise and sexwise distribution of HIV positive cases during the study period. Out of 1341 positive patients 58.9% (790) were male patients and 41.1% ((551)) were female patients with a male to female ratio of 1.41. The HIV-2 prevalence was comparatively more in male patients (6 male Vs 4 female). Statistically significant difference of positivity between the genders is noted with a Z value of 4.7 and P value of 0.0001.

Among different age groups the distribution of HIV serotypes was not uniform. In our study the patients in the age group 31-40 years had maximum number of HIV positive patients (30.6%) followed by age group 41-50 years (26.4%) and more than 50 age group (24.6%). All HIV-2 positive and dual infection patients were above 31 years of age. From all HIV-2 positive patients 50% patients were in age group of 31-40 years. Both the patients having dual infection with HIV-1 and HIV-2 were from age group 41-50 years.

Table 1 : Results of HIV testing over the period of 1 Jan 2014 to 31 Dec 2018

YEAR	TOTAL SAMPLES	TOTAL HIV +	HIV -1+	HIV -1&2 +	HIV -2+
2014	9390	290 (3.08%)	289	1	0
2015	11134	267(2.39%)	264	0	3
2016	13616	274(2.01%)	273	0	1
2017	15793	299(1.89%)	295	1	3
2018	18036	211(1.16%)	208	0	3
TOTAL	**67969**	**1341(1.97%)**	**1329**	**2**	**10**

Table 2: Age wise and Sex wise distribution of HIV seropositive patients

Age group In years	Seropositive Males (n= 790)			Seropositive Females (n=551)			Total
	HIV -1	HIV -1+2	HIV -2	HIV -1	HIV -1+2	HIV -2	
0-10	9	0	0	12	0	0	**21**
11-20	27	0	0	26	0	0	**53**
21-30	90	0	0	81	0	0	**171**
31-40	241	0	3	165	0	2	**411**
41-50	214	1	2	136	1	1	**355**
> 50	202	0	1	126	0	1	**330**
Total	**783**	**1**	**6**	**546**	**1**	**4**	**1341**

Discussion :

As per India estimation 2015 report of NACO, adult HIV prevalence in India was estimated at 0.26% and in Maharashtra higher than national prevalence rate [8]. In prese nt study 1.97% patients were positive for HIV infection [Table1]. Similar results were found in study conducted by Tadokar VS in Pune (1.11%) [9]. In contrast to this in a study conducted in Mumbai by Ingole NA et al (2010) found 7.9% HIV positive cases which is higher than present study[10]. Decreased seroprevalence noted in the present study as compared to Ingole NA study is because of successful

implementation of key strategies under NACP-IV (National AIDS Control Programme - IV) like preventing new infections by sustaining the reach of current interventions and effe ctively addressing emerging epidemics ,achieving universal coverage of prevention of parent to child transmission and providing treatment, care and support to HIV positive patients[8]. This also helped in increasing the awareness among people thus reversing the steady increase in seropositivity at earlier phases as mentioned in study conducted by Bairy I et al (2001) in Manipal[11]. In present study it was observed that over the period of 5 years every year number of samples tested were increased and prevalence of HIV was decreased. This observation matches with data provided by NACO stating that around 66% decline was observed in new infections from 2000 to 2015[12].

Among different age groups the distribution of HIV types was not uniform. In our study all patients infected with HIV-2 were above 31 years age. Majority of HIV-2 patients were from age group 31 -40 years. Remaining HIV-2 positive patients were from age group 41-50 and age group above 50 years [Table 2]. These results are matching with study of Chakravarty J who have reported that the 31–40 years age group to be the most commonly affected [13]. Reason for all HIV-2 positive patients having age above 31 years may be because doubling time of HIV-2 is more than that of HIV-1, HIV-2 is less efficient for sexual transmission, less pathogenic, and slower disease progression which has resulted in longer asymptomatic stage in HIV-2-infected individuals than those infected with HIV-1. Due to longer asymptomatic stage symptoms have occurred at age above 31 years and hence diagnosed at this age by laboratory tests [14,15].

In the present study from all HIV positive patients 58.9% were males and 41.1% were female patients [table 2]. The HIV-2 prevalence was comparatively more in male patients (6 male Vs 4 female). Similar results were seen in study conducted in Mangalore by Jutang Babat and study conducted by Shahapur and Bidri in 2014[16,17]. The reason for Sex differences in HIV arises from combined effects of sex hormones, genetic differences and sociobehavioral & environmental influences [18]. Females having less positive cases in our study might be because of females experience or report fewer symptoms during primary infection which may delay in diagnosis.

As per table 1 compared with HIV-1, HIV-2 positive patients represent very small proportion of all diagnosed HIV patients [0.75% (10) HIV-2 patients Vs 99.1% (1239) HIV-1patients]. Similar results were observed by Sabharwal ER [13]. Where as in studies conducted by Kashyap B (2011) and Tadokar VS (2013) showed only 0.03 % HIV-2 positive results among HIV positive patients which comparatively lower than present study [9,19]. In study conducted by Jutang B et all in Mangalore the results were comparatively higher for HIV-2 (2.8%) [16].

In the present study, out of all samples tested 0.014% of the total samples were positive for HIV-2 [Table1]. Where as in studies conducted in Mumbai by Ingole NA et all (0.14%) and Agrawal S et all (0.35%) showed higher results[10,20]. This might be because of study is conducted in Vidarbha region of Maharashtra where there is less prevalence of HIV-2. Various authors in India have reported that HIV-2 prevalence ranges from 0.14% to 2.8% [9,10,13,16,19,20]. Hence this proves that currently a heterogeneous epidemic of HIV-2 exists in India including variation of results in different regions of individual states. As compared to HIV-1 persistent lower viral load is one reason for a lower incidence rate and the transmission risk seen in HIV-2 infection. In general after seroconversion as compared to HIV-1, HIV-2 the viral load tends to remain low for a longer period. Approximately 5 to 15% of people who are infected with HIV-1 are considered to be long-term non-progressors versus 86 to 95% of people who are infected with HIV-2[21].

The clinical course of HIV-2 infection is generally characterized by a slow disease progression, lower plasma viral loads, slow CD4+ T Lymphocyte (CD4) count depletion, low sexual and vertical transmission, longer asymptomatic stage, and a lower mortality rate than HIV-1 infection [5]. In contrast to HIV-1for treatment of HIV-2 it is suggested that ART should be started at or soon after HIV-2 diagnosis to prevent disease progression and transmission of HIV-2 to others because without effective ART, HIV-2 infection will progress to AIDS and death in the majority of individuals [22]. HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors, Enfuvirtide and some Protease Inhibitors hence these drugs should not be included in ART regimens for HIV-2 infection. Majority of drugs which are currently used for treatment of HIV-1 are resistant to HIV-2 hence guidelines for the use of antiretroviral agents for treatment of HIV-2 infection should be followed meticulously. Initial ART regimens for ART-naive patients who have HIV-2 monoinfection or HIV-1/HIV-2 coinfection should include an integrase strand transfer inhibitor (INSTI) plus two nucleoside reverse transcriptase inhibitors (NRTIs). Persons with HIV-2 who are of childbearing potential require special considerations when choosing a regimen [22]. Patients with hepatitis B virus (HBV)/HIV-2 coinfection should be prescribed ART regimens that contain drugs with activity against both HIV-2 and HBV. Currently, transmitted drug resistance appears to be rare among people with HIV-2 but it may pose threat in future [23].

Unlike persons with HIV-1, persons with HIV-2 should continue to undergo periodic CD4 cell count testing even if their viral loads are persistently suppressed, because disease progression can occur despite an undetectable viral load. Hence for assessment of treatment response to patient monitoring of CD4 cell count should be done.

In India at present in majority of testing centers diagnosis of HIV-2 is done by rapid tests following NACO guidelines and for confirmation sample is sent to higher center for confirmation by more specific tests like Western blot test or nucleic acid test. Hence diagnosis will take extra time for HIV-2 patient and delay in treatment will occur. This implies that in present scenario more accurate rapid test options are needed for diagnosis of HIV-2.

Conclusion :

In present study we conclude that the incidence of HIV-2 and dual infection does occur in Akola but it is comparatively less prevalent than other parts of India. Predominantly Males of age group 31-40 years were most commonly affected. The detailed multicentric survey for HIV-2 should be performed in various parts of India to know current status of HIV-2 infection our country. As HIV-2 may pose serious threat in future, enhancing the diagnosis by detecting HIV-2 by various methods and correct treatment of HIV-2 infection according to new guidelines is the need of time for India. Special guidelines should be made for rapid and confirmatory diagnosis of

HIV-2 patients and ART regimens should be changed according toHIV-2 patient's health condition. Newer FDA approved rapid tests should be used for HIV-2 diagnosis.

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Confict of Interest :

None

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