Research Article

Study of gender difference of opportunistic infections in AIDS patients

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Abstract

Introduction: Concerns about sex-based differences in the course of HIV infection were expressed early in the epidemic. Women appeared to have more rapid progression of illness than men and to present with a different constellation of opportunistic infections than men. Conducting sex comparisons within research studies is important to delineate sex differences or similarities. **Material & Methods**: A prospective cohort study involving HIV infected patients scheduled to start ART, in which 156 male, 82 female and 1 transgender was undertaken to compare the gender difference in age distribution, marital status, presenting symptoms. Structured questionnaires and patients file review were used to collect. data through history, physical examination and laboratory investigations. Gender differences were assessed using chi-square test for categorical data. **Results:** In the study population 239 patients who fulfilled NACO guidelines for AIDS were included, 156 men and 82 women. Fever was the commonest presenting symptom (57.32%) in both males and females, 61.53% of males and 48.78% females presented with fever. The most frequent AIDS Defining Infections were tuberculosis (42.25%) and candidiasis (22.6%). Pulmonary Tuberculosis, Tubercular meningitis were significantly higher in males compared to females. Herpes simplex (P value 0.007) and non specific dermatitis showed statistically significantly higher in females compared to males in occurrence rate. **Conclusion**: Evaluation of differences between human immunodeficiency virus (HIV)-infected men and women in antiretroviral therapy (ART) enrollment characteristics and outcomes might identify opportunities to improve ART program, patient outcomes and prevention impact. We studied gender differences in opportunistic infections in AIDS patient.

Keywords- HIV, Opportunistic infection, Gender, HAART

Introduction

The progression rates to AIDS and clinical manifestations of diseases associated with HIV infection might differ between women and men because of biological and socioeconomic factors [1]. Previous investigations found different rates of HIV disease progression and of virological and immunological response to antiretroviral therapy among HIV-infected women compared with men [2,3]. The HIV epidemic in Asia remains concentrated in nature, affecting mostly higher risk subgroups, including men who have sex with men (MSM) and transgender women (TG), people who inject drugs (PWID), and female sex workers (FSW)[4]. These epidemiological features have considerable implications for the implementation of prevention intervention trials and further implementation of prevention policies in the region.

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Addressing gender inequalities is central to improving the sexual and reproductive health outcomes and more broadly the wellbeing of women living with HIV. Programmes that go beyond a narrow biomedical /clinical approach and address the social and structural context of women's lives can also maximize the benefits of HIV prevention, treatment, care and support [5].

Men living with HIV have consistently and significantly greater hazards of all-cause mortality compared with women while on antiretroviral therapy [6]. This effect persists over time on treatment.

The clinical and population-level prevention benefits of antiretroviral therapy will only be realized if programmes can improve male engagement, diagnosis, earlier initiation of therapy, clinical outcomes and can support long-term adherence and retention [6]. India has the third largest HIV epidemic in the world, In 2015,

HIV prevalence in India was an estimated 0.26%. This figure is small compared to most other middle-income countries but because of India's huge population (1.2 billion) this equates to 2.1 million people living with HIV. In the same year, an estimated 68,000 people died from AIDS-related illnesses [7]. Overall, India's HIV epidemic is slowing down, with a 32% decline in new HIV infections (86,000 in 2015), and a 54% decline in AIDS-related deaths between 2007 and 2015[7].

The current study was developed to examine gender-based differences in opportunistic infections after initiation of ART in a resource-limited setting. These data will enable clinicians to develop more effective and better tolerated treatment strategies for HIV-infected men and women. In light of the increasing feminization of the HIV epidemic in the developing world, this study is timely in assessing gender-based differences in the era of highly active ART (HAART).

Material & Methods

The study was done prospectively from September 2010 to September 2011 at Index Medical College Indore. The study was carried out among 156 male, 82 female, and 1 transgender who reported to ART centre of Medical College, Indore and who fulfilled the NACO guidelines for diagnosis of AIDS

Study Design- Prospective cohort study.

Inclusion Criteria: HIV positive individuals by ELISA fulfilling NACO criteria with Age group > 15 yrs including both male and female.

Exclusion Criteria: Individuals with HIV1&2 non reactive and Age below 15 yrs.

Data collection- Oral consent was obtained according to the Proforma. Patients underwent a detailed history, physical examination and routine laboratory investigations. Specific laboratory investigations for the diagnosis of appropriate opportunistic infections are Microscopic examination of sputum stained by the Ziehl-Neelsen (ZN) method is the diagnostic test of choice for tuberculosis, A presumptive diagnosis of pneumocyctis carinii can be made in the presence of clinical symptoms, low CD4 count/presence of oral candidiasis and suboptimal prophylaxis in the past ,definitive diagnosis of Pneumocystis jiroveci pneumonia is confirmed by demonstration of the organism in pulmonary secretions, Diagnosis for Cryptococcus is confirmed when Cryptococcus is identified in the CSF or CNS tissue by positive culture or histopathology. Serum IgG and IgM anti-Toxoplasma antibodies can be estimated for toxoplasmosis. CMV viraemia can be detected by PCR, antigen assays or blood culture, Diagnosis for MAC is considered probable if MAC is cultured from the bronchopulmonary, gastrointestinal, skin surface or other non-sterile sites (as the sole pathogen) and histopathological confirmation of AFB/MAC is obtained from the tissue specimen from which the culture was obtained. Diagnosis for candidiasis was usually clinical and based on the characteristic appearance of the lesions and the ease with which the superficial whitish plaques can be scraped off. Microscopical examination of the scrapings using a potassium hydroxide (KOH) preparation shows yeast forms for candidiasis, Molloscum Contagiosum Diagnosis was usually based on the clinical appearance. Giant confluent lesions may have a bizarre appearance and require biopsy. Herpes Zoster and herpes simplex was diagnosed empirically based on the appearance of characteristic lesions. Pelvic Inflammatory Diseases are diagnosed by Pelvic ultrasound Vaginosis/ Vulvo vaginitis- microscopy of vaginal discharge and biopsy for Lymphoma.

Short-term memory losses, depressed affect, unexplained seizures, CT and MRI scans show diffuse cortical loss with prominent sulci ("walnut sign") are for AIDS Dementia Complex (ADC)/HIV Encephalopathy

Statistical Analysis-Chi-square and Fisher exact test have been used to test the significance of proportions of diagnosis between male and Female.

Statistical software-The Statistical software SPSS 11.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Results

The study was done prospectively from September 2010 to September 2011 at Index Medical College Indore. The study was carried out among 156 male, 82 female, and 1 transgender who reported to ART centre of Medical College, Indore and who fulfilled the NACO guidelines for diagnosis of AIDS.

Table-1: Route of Transmission.

Route of transmission	Male	Female	Transgender	Total
Heterosexual	143	69	0	212
MSM	0	0	1	1
Intravenous Drug users	0	0	0	0
Blood Transfusion	0	7	0	7
Probable unsafe injection	0	0	0	0
Unknown	13	6	0	19
Total	**156**	**82**	**1**	**239**

In the study population the predominant mode of acquiring HIV infection was heterosexual contact (88.70%). Other routes of transmission as per our study are Blood transfusion (2.92%), homosexual transmission (0.41%), and Unknown (7.94%).

Table-2: Presenting Symptoms of Patients.

Symptoms	Male	Female	Transgender	Total
Fever (> 1 month)	96	40	1	137
Weight Loss	51	29	0	80
Asthenia	49	23	0	72
Cough	47	24	0	71
Chronic Diarrhea	35	15	0	50
White discharge per vaginal	0	3	0	3
Altered sensorium	3	0	0	3
Difficulty in swallowing	6	1	1	8
Itching	1	5	0	6
Chest pain	1	0	1	1
Decreased vision	1	0	0	1
Urethral discharge	1	0	0	1
Sore throat	3	1	0	4

Fever was the commonest presenting symptom (57.32%) in both males and females, 61.53% of males and 48.78% females presented with fever. The major symptoms seen among the AIDS patients were weight loss(33.4%), asthenia (30.1%) and diarrhea (29.70%) were common symptoms.

Table-3: Presenting Signs of Patients.

Signs	Male	Female	Transgender	Total
Oral Thrush	33	20	1	54
Pallor	11	6	0	17
Genital Ulcers	2	9	0	11
Lymphadenopathy	7	1	0	8
Vesicobullous lesion	4	2	0	6
Meningeal signs	7	0	0	0
Skin rash	1	5	0	6
Splenomegaly	1	0	0	1
Pleural effusion	1	0	0	1
Fluid thrill	0	1	0	1

Oral candidiasis (22.6%), Pallor (7.1%) were the commonest presenting signs. There were no difference in the clinical signs at presentation except for lymphadenopathy, meningeal signs in the males and skin rashes, genital ulcers in the females.

Table-4: Opportunistic Infections.

Disease	Male	Female	Transgender (%)	Total	P
Total Tuberculosis	72	29	0	101	0.11
Pulmonary TB	36	27	0 (0%)	90	0.001*
Extra pulmonary tuberculosis					
A. TB lymphadenitis	6	1	0	7	0.25
B. Tubercular meningitis	3	0	0	3	0.003*
C. Koch's abdomen	1	1	0	2	0.65
D. Pott's spine	1	0	0	1	0.46
E. Tubercular ascites	0	1	0	1	0.17
F. Tubercular pleural effusion	1	0	0	1	0.46
Oropharyngeal Candidiasis	33	21	0	54	0.49
Esophageal Candidiasis	6	1	1	8	0.257
Herpes Genitalis	5	10	0	15	0.007*
Cryptococal meningitis	2	0	0	2	0.19
CMV retinitis	1	0	0	1	0.46
Recurrent Bacterial Pneumonia	1	3	0	4	0.37
Pelvic Inflammatory disease	0	3	0	3	0.01*
Non specific dermatitis	1	5	0	6	0.01*
Non specific lymphadenopathy	1	0	0	1	0.46

The most frequent AIDS Defining Infections were tuberculosis (42.25%), and Candidiasis (22.6%). The other conditions seen in this study were Herpes simplex (6.28%), nonspecific dermatitis (2.51%), recurrent bacterial pneumonia (1.67%) Pelvic inflammatory disease (1.25%), Cryptococcal meningitis (0.8%), CMV retinitis (0.4%) and non specific lymphadenopathy (0.4%). The disease pattern in our study has demonstrated some gender differences. Herpes simplex (12.2% vs 3.2%), recurrent bacterial pneumonia (3.6% vs 0.66%), and non specific dermatitis (6% vs 0.64%) were more frequent in women. Men had higher incidence of Pulmonary Tuberculosis (40.4% vs 32.9%), Tubercular lymphadenitis (3.8% vs 1.2%), Tubercular meningitis (1.9% vs 0%), Esophageal Candidiasis (3.8% vs 1.2%). Pulmonary Tuberculosis (P value 0.001), Tubercular meningitis (P value 0.003), Herpes simplex (P value 0.007) and non specific dermatitis (P value 0.01) showed statistically significant differences in occurrence rate between women and men.

Discussion

India has the third largest HIV epidemic in the world. In 2015, HIV prevalence in India was an estimated 0.26% [7]. The HIV epidemic in India is driven by heterosexual sex, which accounted for 87% of new infections in 2015. However, the epidemic is concentrated among key affected populations such as sex workers. The vulnerabilities that drive the epidemic are different in different parts of the country [8].The five states with the highest HIV prevalence (Manipur, Mizoram, Nagaland, Andhra Pradesh and Karnataka) are in the south or east of the country. Some states in the north and northeast of the country have also reported rising HIV prevalence [7].

It appears that certain HIV-associated opportunistic infections disproportionately affect either men or women regardless of treatment status, which may reflect underlying biological differences between men and women. During the first year after initiating HAART, men experienced a significantly higher incidence of tuberculosis. In a prior study at YRG CARE, a high incidence of IRS was reported in the male population with a high background rate of tuberculosis [9]. A study from South Africa found that although incident tuberculosis rates did not differ by gender, incident tuberculosis rates after initiating HAART were associated with a pretreatment CD4 count of <100 cell/μL and advanced immunodeficiency[10].

Today, nearly half of the people living with HIV globally are women[11].The rising number of women living with HIV requires greater clinical investigations examining gender-based differences in treatment and outcome in the era of antiretroviral therapy (ART), particularly because generic medication has dramatically reduced the cost of treatment. Gender-based differences in pharmacokinetics, side effect profiles, and access to and efficacy of these medications may limit the generalizability of many clinical studies to women [12]. Observational studies conducted in the developed world

have documented possible virological, immunological, and clinical differences between men and women receiving ART [13,14,15], which may be attributable to social and biological differences[12-16].

Fever was the commonest presenting symptom (57.32%) in both males and females, 61.53% of males and 48.78% females presented with fever. The most frequent AIDS Defining Infections were tuberculosis (42.25%) and candidiasis (22.6%). Pulmonary Tuberculosis & Tubercular meningitis were significantly higher in males compared to females. Herpes simplex (P value 0.007) and non specific dermatitis showed statistically significantly higher in females compared to males in occurrence rate. Similarly Studies indicate that asymptomatic Indian women may be tested for HIV earlier, after their spouses are diagnosed at a more advanced stage of HIV and seek clinical care for an opportunistic infection [17]. One of the major reasons why women appeared to come earlier in the course of their HIV infection was that many women were identified as HIV infected after their husbands developed advanced disease. Because the women had earlier access to treatment and clinical care, fewer women than men died in the first year after initiating therapy. Additionally, because of the increasing availability of antenatal testing as part of ongoing expansion in voluntary counseling and testing[18], Indian women who learned their serostatus at the time of pregnancy may have then reported to clinical care earlier than men. However, many Indian women at risk for HIV may not be seeking testing or may not seek continued clinical care after a positive HIV test because of concerns about confidentiality and fear of negative reactions from husbands, parents, and community [19,20].

It appears that certain HIV-associated opportunistic infections disproportionately affect either men or women regardless of treatment status, which may reflect underlying biological differences between men and women. During the first year after initiating HAART, men experienced a significantly higher incidence of tuberculosis. In a prior study at YRG CARE, a high incidence of IRS was reported in the male population with a high background rate of tuberculosis [21]. A study from South Africa found that although incident tuberculosis rates did not differ by gender, incident tuberculosis rates after initiating HAART were associated with a pretreatment CD4 count of <100 cell/μL and advanced immunodeficiency[22]. In this study, The most frequent AIDS Defining Infections were tuberculosis (42.25%), and Candidiasis (22.6%). The other conditions seen in this study were Herpes simplex (6.28%), nonspecific dermatitis (2.51%), Recurrent bacterial pneumonia (1.67%) Pelvic inflammatory disease (1.25%), Cryptococcal meningitis (0.8%), CMV retinitis (0.4%) and non specific lymphadenopathy (0.4%). The disease pattern in our study has demonstrated some gender differences, results were similar to study done by Kumarasamy N et al[23].

Conclusion

The present study highlighted significant gender-based differences in opportunistic infections. These data will enable clinicians to develop more effective and better tolerated treatment strategies for HIV-infected men and women. In light of the increasing feminization of the HIV epidemic in the developing world, this study is timely in assessing gender-based differences in the era of highly active ART (HAART).

Future studies should examine whether clinical management strategies should be different for men and women in resource-limited settings. The study recommended further intervention programmes targeting healthcare providers to address fear of transmission, improve universal precaution skills, and involve people living with HIV at all stages of the intervention to reduce symbolic stigma and ensure that relevant patient interaction skills are taught.

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