Molecular Epidemiology of Human Immunodeficiency Virus Infection and Aids

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Abstract: Epidemiological data indicate that globally the spread of HIV peaked in 1996, when 3.5 million new HIV infections occurred. Similarly, maximum number of AIDS related deaths were in 2004 when an estimated 2.2 million people died. Globally, 65 million people have been infected by HIV out of which 30 million have died since the first case was reported in 1981. Sub-Saharan Africa is the most heavily affected region with 67% of the global burden where heterosexual spread in the general population is the main mode of transmission [1, 2]. Male to male sex, injection drug use, and sex work are the predominant risk factors in most other regions. The global prevalence of HIV-1 has stabilized at 0.8%, and number of people living with HIV in 2008 was 33.4 million among which 31.3 million were adults including 5.7 million women. Number of infected children under 15 years was 2.1 million. AIDS death toll in 2008 was 2 million and the number of new infection was 2.7 million. In 2008, the estimated number of new HIV infections was approximately 30% lower than at the epidemic's peak in 1996. The estimated number of AIDS related deaths in 2008 was 2.0 million (10% lower than in 2004) [3]. Recent HIV epidemiologic research findings provide new insights into the role of HIV viral load, co-infection with sexually transmitted infections, male circumcision, antiretroviral treatment, serosorting and superinfection in HIV transmission and prevention [4].

GLOBAL EPIDEMIOLOGY OF HIV

According to 2009 AIDS epidemic update report of the Joint United Nations Program on HIV/AIDS and the World Health Organization (WHO), from 2001 to 2008 new HIV infections have dropped by 17% [5]. The rate of new HIV infection has dropped in East Asia, sub-Saharan Africa and South and South East Asia by 25%, 15% and 10% respectively. In Eastern Europe it has leveled off, while in some countries such as China, India, Pakistan, Nepal and Bangladesh it looks like the new HIV infection rate is on the rise. Despite such drop in infection rates 2.7 million people became infected with the virus in 2008. In the US due to routine HIV screening of pregnant women, use of antiretroviral (ARV) drugs for treatment and prophylaxis, avoidance of breastfeeding, and use of elective cesarean delivery at appropriate time, rates of HIV transmission during pregnancy, labor or delivery from mothers infected with HIV have been reduced to less than 2%, compared with transmission rates of 25%–30% with no interventions [7].

The face of the HIV epidemic is changing and total number of people living with HIV is rising which reflects the combined effects of high rates of new HIV infections and the beneficial impact of antiretroviral therapy and better management of opportunistic infections prolonging survival. World Health Organization predicts that despite these successes AIDS-related illnesses will continue to remain one of the leading causes of death globally in the coming decades [8].

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Diverse risk behaviors are incriminated in the HIV-1 transmission in different regions of the world and, within the same region, multiple transmission routes can be involved in spreading the epidemic. Molecular studies are providing useful information about host parasite relationship such as the co-circulation of B subtype among IDUs and CRF01_AE (originally defined as E subtype) among heterosexuals in Thailand [9] ; the segregation of B subtype in homosexuals and C subtype in heterosexuals in South Africa [10] ; two concurrent epidemics in Argentina among MSM, dominated by the B subtype, and among heterosexuals and IDUs, by BF recombinants [11]. In Europe, the B subtype has dominated among the IDUs and Homosexual risk groups, non-B sub-types and CRFs are progressively introduced in heterosexual transmission between migrants/immigrants from endemic regions [12]. All these observations, reported in different phases of the HIV-1 epidemics around the world, may suggest different biological properties for the subtypes, resulting in their segregation among individuals with different risk behaviors for HIV-1 infections.

Majority (> 90%) of HIV-1 infections are caused by HIV-1 group M. Several genetically distinct lineages (sub-types or clades) within Group M have also been identified. These include subtype designations A, B, C, D, F, G, H, J and K. The classification of HIV strains into subtypes and CRFs is a complex issue and the definitions are subject to change as new discoveries are made. Some scientists label subtypes A1, A2, A3, F1 and F2 instead of A and F, though others regard the former as sub-subtypes [13]. Sequence variation with in a subtype may be up to 15% in *gag* and 30% in *env* region while inter-subtype variation may be 30-40% in the same two genes [14]. Two types of genetic recombinant

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forms have been identified namely, circulating recombinant forms (CRF) and the unique recombinant forms (URF). Many of these new strains do not survive for long, but those that infect at least three epidemiologically unlinked people, and characterized by full-length genome sequencing, are designated as circulating recombinant forms (CRFs) (Fig. **1**). There are currently more than 43 recognized mosaic viruses or CRFs whose origin can be tracked in areas where the parental strains are co-circulating [15].

Contact tracing along with phylogenetic analysis may be useful in tracking the infection and identifying the drivers of transmission and calculating the geospatial relationship. It also provides suggestive information about clusters of infection which is useful for public health interventions and may also be used to calculate the timing of exposure and transmission during consensual relationship. Molecular epidemiological studies are continuously required to trace the epidemic, viral genetic diversity, antiviral resistance, vaccine development and therapeutic tools necessary to control the spread of the current pandemic [16].

HIV EPIDEMIOLOGY IN PAKISTAN

Until 2004, Pakistan was considered a low prevalence high-risk country with respect to HIV infection. The situation, however, has been changing rapidly since 2004 due to emergence of concentrated HIV epidemic among Injection Drug Users (IDUs) followed by a similar trend in male sex workers. The heterogeneity and interlinking of injecting drug user and high risk sexual practices combined with low levels of HIV knowledge about prevention, and high levels of other sexually transmitted infections (STIs), indicate that there is a great potential for rapid spread of HIV through the bridging population [17, 18].

The first few locally transmitted cases of HIV infection in Pakistan were identified from Karachi in 1985 among family of a drug addict (husband, wife and son) and a paid blood donor [19]. Since then a number of studies have been conducted and HIV infections reported among various vulnerable groups. Based on estimates of the vulnerable groups, sentinel surveillance and reported HIV cases, it is

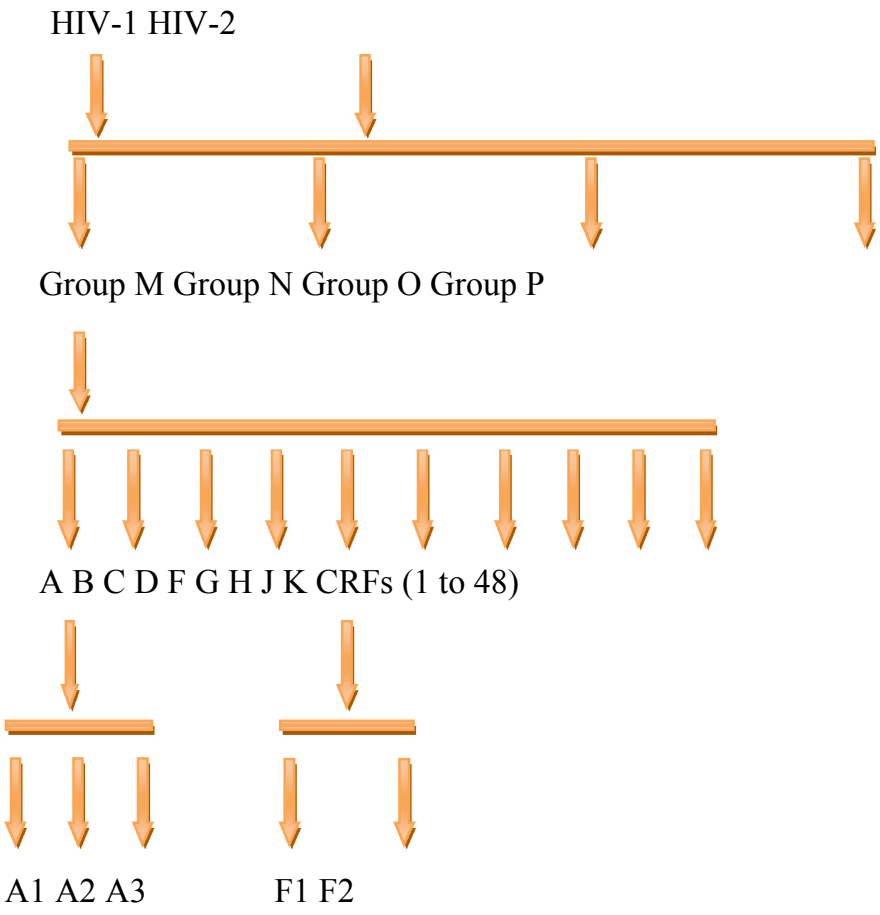

Fig. (1). HIV Genotypes.

estimated that approximately 97,600 persons or 0.1% of adult population are infected with HIV in Pakistan [20].

The first major reported clustering of HIV among IDUs was in 2003-4 in the city of Larkana in Sindh province, where 10% of 175 IDUs were found HIV positive [21]. In another study in 2004, 8.3% of the 3,175 IDUs tested in Larkana were positive. National Study of RTI & STI in 2005 reported HIV prevalence among IDUs in Karachi of 23%. Second Generation HIV/AIDS Surveillance Project (HASP) of high risk behavioral groups demonstrated HIV prevalence among IDUs was more than 5% in five out of eight cities including Karachi 26.5%, Hyderabad 18.3%, Sukkur 19.6%, Quetta 9.1% and Faisalabad 13.3%. Data from SGS round III (2008) depicted a gloomy picture showing HIV prévalence of 51.5% among IDUs in Sargodha and an increasing prevalence in Karachi from 26.5 to 30%, Hyderabad from 18.3 to 29.75% and Lahore from 3 to 6.5% [22, 23].

The MSM community is heterogeneous and includes Hijras (biological males who are usually fully castrated), Zenanas (transvestites who usually dress as women), masseurs (Malishyas) and other males who desire male to male sex [24]. Many sell sex (Male Sex Workers or MSW) and have multiple sexual partners. In sub-continent Hijra are part of ancient and secretive community of transsexuals, hermaphrodites and eunuchs. The 2004 STI survey found that 4% of MSMs and 2% of the Hijras in Karachi were infected with HIV. Syphilis rates were also high with 38% of MSMs and 60% of Hijras found infected [22]. Recently there has been clustering of HIV cases among transgender (hijras) MSWs in Larkana where 27.6% were found HIV positive out of 200 subjects tested. HIV prevalence among female sex workers is still less than 0.1% which is equal to general population [23].

Refugees and migrants are also at increased risk of HIV infection [25]. Afghan refugees fled to Pakistan in several waves starting from 1979. One major settlement of Afghani settlers is at Soharab Goth a refugee settlement at the outskirts of Karachi. It is also well known that injudicious use of injections and reuse of syringes is also very common in these settlements in addition to other factors such as drug abuse and sexual contact. All these factors contribute to the increased risk of HIV in this community.

Molecular epidemiology studies are a recent phenomenon in Pakistan. An earlier molecular study of IDUs identified HIV subtype A in all the samples tested [26]. We found that HIV epidemic in the Pakistani Males having Sex with Males (MSM) is caused by HIV subtypes A and G, as well as CRFs AE and AG. The analysis of gene sequences from IDUs, MSM and MSM families revealed a possible bridging of HIV infection from the core high risk group of IDUs, through MSM and M-IDU (MSM practicing intravenous drug use), into the spouses and children of MSM [27].

All these risk factors and behaviors ultimately lead to spill over of HIV infection from high risk groups to general population through bridging population. A number of cases of HIV infection have been detected in population not considered to be at risk because of their own behaviors. This phenomenon of HIV spread into general population is a great threat to the health of our nation. HIV prevention programs need to be tailored keeping in view these epidemiological factors, if Pakistan has to maintain its status as a low HIV prevalence country.

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