ORIGINAL ARTICLE

Effectiveness of HIV Pre-Exposure Prophylaxis (PrEP) in Pakistan

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ABSTRACT

Objective: To evaluate the effectiveness of HIV Pre-Exposure Prophylaxis (PrEP) in HIV Clinic of a tertiary care hospital in Pakistan.

Study Design: A descriptive study covering the data of clients who were offered PrEP.

Place and Duration of Study: HIV treatment center Pakistan Institute of Medical Sciences (PIMS) Islamabad, Pakistan, from October 2019 to September 2022.

Materials and Methods: Total of 118 people without HIV from various high-risk population groups were reported in HIV treatment center PIMS during a period of 3 years including 39 females from serodiscordant couples, 16 transgender females, and 63 men having sex with men (MSM). All of them were given oral PrEP after necessary screening, investigations, and evaluation. These clients were prescribed a fixed drug combination of Tenofovir/Lamivudine (TDF/3TC) one tablet daily as PrEP. The alternate regimen used was Event-driven PrEP (EDP) for MSM. Monthly follow-up was performed, and all patients were found to be HIV negative.

Results: All 118 clients receiving PrEP remained seronegative on regular monthly follow-ups after a sufficiently long period of unsafe sexual practices that frequently exposed them to HIV-positive sex partners. Based on their age mean age of the clients in young group below 35 years was 27 $\pm$ 6, all 62 young clients had 100% protection. Similarly, 41 middle aged (mean age 43 $\pm$ 6) and 15 old clients (mean age 56 $\pm$ 5) had 100% protection with PrEP. Six women from serodiscordant couples while receiving PrEP became pregnant with partners who had completely suppressed viral load (<50 copies).

Conclusion: Oral PrEP has offered complete protection to all seronegative individuals belonging to high-risk population groups despite their frequent exposure to HIV-positive partners. All 118 individuals who received PrEP remained seronegative.

Key Words: *HIV, Pre-exposure prophylaxis, Serodiscordant Couples, Event-driven PrEP. HIV Prevention, MS.*

Introduction

HIV/AIDS is a global public health problem. There is no cure for the disease and once the HIV infection is acquired by an individual, he needs life-long treatment with ARVs to keep the viral load suppressed.[1 6] Most common ways for HIV transmission are unsafe sex practices and injection drug use with shared syringes. Despite a global awareness campaign, many people tend to ignore the risks involved and indulge in unsafe sex practices or share syringes with other injection drug users**.** A systematic review of published and unpublished data from randomized trials found no significant differences in the efficacy of lamivudine and emtricitabine, consistent with very similar chemical structures of these two nucleoside analogues.[13] There has been a growing need to find effective methods to stop spread of HIV infection to healthy individuals. PrEP is an effective and safe method of prevention of HIV transmission in high-risk population groups. While the incidence of HIV has declined worldwide over the past decade, many new HIV infections occur globally highlighting the ongoing need for new and effective HIV prevention initiatives. Oral pre-exposure prophylaxis of HIV (PrEP) is the use of antiretroviral drugs (ARVs) by HIV seronegative individuals from high-risk population groups to block the acquisition of HIV[1]. The US Food and Drug Administration approved TDF with emtricitabine (FTC) for oral PrEP in 2012. In 2015, WHO recommended once-daily oral PrEP to population susceptible of HIV. However, for MSM,

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the 2019 WHO guidance include options for event driven dosing (on demand PrEP).[14] Oral PrEP trials have shown evidence of effectiveness in certain high-risk population groups in society including serodiscordant couples, MSM, transgender females, and injection drug users (IDUs)[5]. In Pakistan, the PrEP regimen consists of a fixed-dose combination of Tenofovir with Lamivudine in place of Emtricitabine. Oral PrEP containing TDF co-formulated with FTC[3] or 3TC is recommended as an additional prevention option for persons at substantial risk of HIV infection by both WHO and the US President's Emergency Plan for AIDS Relief (PEPFAR).[21]Clinically 3TC is interchangeable with FTC for PrEP given comparable pharmacologic equivalence, resistance, and toxicity patterns[2], and indirect clinical trial evidence from TDF-containing studies.[12] PrEP has provided significant protection to these high-risk population groups[4]. Daily oral PrEP with tenofovir/emtricitabine is highly efficacious in preventing HIV infection with high adherence and safe to use during pregnancy and breast-feeding.[9] Therefore we design our study to evaluate the effectiveness of HIV Pre-Exposure Prophylaxis (PrEP) in HIV Clinic of a tertiary care hospital in Pakistan.

Materials and Methods

This descriptive study was carried out in a tertiary care hospital in the Federal Capital of Pakistan after obtaining approval from Institutional Ethical Committee Ref no 6/9/22 (1). This study covers a period of 3 years from October 2019 to September 2022. Behavioral therapy was conducted by experienced counselors of the HIV Clinic before initiating the PrEP therapy, and biomedical interventions[8] were explained to the clients. As per WHO guidelines, seronegative males, females, and transgender women of all ages from key population groups and those with unsafe sex practices were offered PrEP. During the last 3 years, 118 individuals from high-risk population groups were given PrEP including 63 MSM, 39 female members of serodiscordant couples, and 16 transgender females.[15] Selection criteria were strictly followed as per the WHO guidelines for offering PrEP. After initiation of ARVs, regular follow-up of individuals was ensured and compliance/adverse effects as well as the HIV-negative status of clients monitored. The following three eligibility criteria were necessary for offering PrEP: Confirmed HIV-negative status, no signs, and symptoms of acute HIV infection, and acknowledged being at substantial risk for HIV. Exclusion criteria for PrEP include HIV infection, Adolescents less than 35 kg, impaired renal function, Allergy, or contraindication to any drug in the PrEP regimen, Refusal to follow up, and Pregnancy.

PrEP Regimen:

I. FDC (Fixed Dose Combination; Lamivudine 300 mg + Tenofovir (TDF) 300 mg
II. Daily Dosing PrEP
III. EDP (Event Driven PrEP) or 3-day PrEP[15]

Following lab investigations were performed to determine the eligibility status of the individual for PrEP:-

1. Rapid test: Negative
2. RFTs: Normal
3. Pregnancy test for the female client: Negative

Clients receiving PrEP were divided into three groups based on gender i.e., males, females, and transgender women. Another division was made based on age i.e., clients less than 35 years, 35 to 60 years, and more than 60 years. Another grouping was done according to the high-risk population groups i.e., MSM, HIV-negative members of serodiscordant couples, and heterosexual sex workers. Follow-up was done regularly for an uninterrupted supply of medicines. A rapid test was performed after every 3 months. Serum creatinine was also checked after every 3 months. PrEP was discontinued in 6 females temporarily due to pregnancy and resumed after childbirth with the mother's consent.

Results

A total of 118 seronegative clients from high-risk population groups were given PrEP[7]. All individuals remained seronegative on regular follow-up tests with rapid test kits. These clients were MSM, female members of serodiscordant couples, and transgender women.

The total number of clients were divided in three groups based on their ages : <35 Y, 35-50 Y, and >50 y. Based on their age (Table-1), mean age of the clients in young group below 35 years was 27 $\pm$ 6, all 62 young clients had 100% protection. Similarly, 41 middle aged (mean age 43 $\pm$ 6) and 15 old clients (mean age 56 $\pm$ 5) had 100% protection with PrEP.

Another comparison based on gender (Table -1)

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Table I: Age, Gender, and Risk Population-Based Data of Study Participants (n= 118)

Age Groups			Gender			Risk Population group				
<35 Y	35-50 Y	>50 y	Male	Female	TG	MSM	Serdiscordant	Transgender Women	IDUs	Female sex workers
62	41	15	63	39	16	63	39	16	0	0

MSM: Men who have sex with Men
IDU: Injection drug use.

shows all three groups have 100% protection from HIV with PrEP. Another group based on high-risk population groups (Figure-1) shows complete protection for MSM, discordant couples and transgenders. However, there was no client in IDUs group since no one opted to get PrEP from IDUs, those who are registered with HIV Clinic are all HIV positive and do not fulfill criteria to administer PrEP.

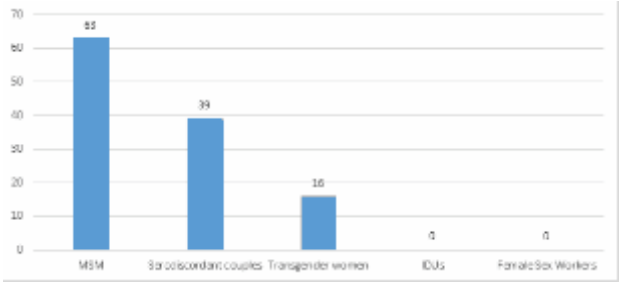

Figure 1: Comparison of Prep Clients According to High-Risk Population Groups

Discussion

The Centers for Disease Control and Prevention (CDC) reports that studies on PrEP effectiveness have shown that consistent use of PrEP reduces the risk of getting HIV from sex by about 99%.[15] Certain HIV seronegative population groups are more at risk of acquiring HIV infection because of their marital relationship with an HIV-positive spouse or due to their adopted unsafe practices. Such individuals need protection against the potential transmission of infection by physical methods like the use of condoms and avoidance of unsafe sex practices.[10,19] However, this approach is seldom adopted either by these vulnerable people themselves or by their sex partners resulting in the transmission of HIV to a previously uninfected individual. To avoid this risk, PrEP was introduced by FDA and WHO. PrEP is offered to people who are HIV-negative but are at risk of getting HIV through sex or injection drug use, they take ARVs daily to prevent HIV infection. The fixed drug combination of TDF (300 mg) with 3TC (300 mg) is used mostly as a daily single dose[12]. In the case of MSM, EDP is offered as it needs less frequent dosing and provides an option to the individual to administer the PrEP as per his sexual practices[11]. This regimen is supposed to provide better compliance by the client.[17]

An uninfected member of a serodiscordant couple is offered PrEP after behavioral therapy and counseling of the HIV-positive partner to use ARVs and ensure compliance to keep the viral load at an undetectable level (<50 copies on PCR). In case the female is on PrEP and the couple meets the above criteria, then pregnancy is permitted, and according to WHO guidelines pregnant female is given a choice to discontinue PrEP to avoid any adverse effects on the fetus. PrEP is restored after the delivery of the baby. In our study 6 females from serodiscordant couples became pregnant, their PrEP was stopped during pregnancy and all 6 delivered healthy babies. Their PrEP was restored after delivery and all of them were advised to breastfeed their babies since it is a safe practice.[9]

Transgender female clients were advised daily PrEP regimen because of their unsafe practice and a lifestyle that makes them vulnerable to acquiring HIV infection from multiple sex partners. These clients are mostly registered with NGOs due to which they remain under continuous surveillance by the dedicated staff. Their compliance is good and regular follow-up is expected.

Most clients from the MSM group were referred by NGOs that deal with HIV/AIDS population. They are reluctant to show up and need a lot of persuasion, encouragement, and a guarantee of complete confidentiality to convince them for starting PrEP. Due to efforts of NGOs, this group constitutes the biggest proportion of clients receiving PrEP from HIV treatment center PIMS.

It was noted with interest while conducting the analysis that no client was registered in PrEP from population groups like IDUs and female sex workers. On further investigation main reason was the fact that IDUs are mostly HIV positive and therefore do not fit into the inclusion criteria for PrEP. Moreover, some MSM may be using injection drugs but there is a possibility that they did not disclose because most of these clients were reluctant to seek PrEP and reported voluntarily only due to motivation by NGOs

to use PrEP. Female sex workers do not agree to document their activities by disclosing their profession or activities.[20]

PrEP has been providing safety to 118 registered clients since 2019. Some of them are using ARVs for 2 to 3 years and are still HIV-negative. The analysis of the study and results obtained show complete safety to the clients on PrEP. Their regular follow-up and investigations provide a pattern of the efficacy of ARVs as well as the safety of the regimen used. It has been a useful tool so far for the prevention of HIV transmission to vulnerable population groups who are frequently exposed to sexual contact with HIV-positive patients.

Conclusion

Results compiled from this study showed that PrEP therapy is highly effective to prevent HIV in different risk groups of different ages. High-risk population groups are benefiting from this program which is successfully working since October 2019. There were no reports of any serious side effects of ARVs, no therapeutic failure, no case of loss to follow-up, no issue of compliance, and no evidence of resistance to used drugs. There is a need to initiate PrEP in other HIV Clinics in Pakistan after a successful launch in Islamabad.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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Authors have declared no specific grant for this research from any funding agency in public, commercial or nonprofit sector.

DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.