Adherence, virologic failure, and severe mutations - Need for 2nd line HAART in India

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Background
• Since 2003, there has been a massive global scale-up in access to highly active antiretroviral therapy (HAART), due to a dramatic decrease in prices and the increased political will to provide treatment in resource-limited settings [1].
• The WHO recommends semi-annual monitoring of CD4 cell counts after initiating HAART, due to the high cost and infrastructure required for viral load testing. However, immunologic failure and clinical events after initiating HAART can occur 6 months to 2 years after virologic failure [2], leading to a delay in detecting this failure. Additionally, genotypic mutations can occur at low levels of viremia [3].
• Studies have documented that continuing failed HAART regimens can lead to the accumulation of genotypic mutations, which may limit options for second-line treatment regimens [4, 5].
• Understanding patterns of mutations among patients who are receiving first-line HAART and immunological monitoring can assist clinicians in selecting second-line regimens in resource-limited settings with already constrained second-line treatment options.
• Genotypic mutations to antiretroviral drugs have been described among ART-naïve Indian populations. Though there has been a dramatic increase in the number of individuals receiving antiretroviral therapy in India, relatively little is known about the development of drug resistance among patients on failing first-line HAART.

Methods
Participants: 213 patients were recruited from one private (n=83) and one government-run (n=130) ART clinic in Bangalore.
Study Design: Observational cohort study. Participants will be followed every 3 months for 2 years.
Procedures: 1) An interviewer-administered survey is administered to assess adherence patterns and individual, social, and regimen-specific factors that may impact adherence.
2) Study phlebotomists collect blood samples every 6 months, which are analyzed for viral load and CD4/CD8 counts. All samples with VL >1,000 copies/ml are sent for viral genotyping.

Measures: Self-reported adherence in the past 4 days, 1 week, & 1 month, using ACTG scale; # missed pills/total pills, and a Visual Analogue Scale; viral load, CD4/CD8, ART regimen, and health history; Demographic information, individual-, social-, and regimen-specific adherence barriers, depression, medication side effects, internalized AIDS stigma, and avoidant coping. All behavioral and psychosocial variables used either "ever" or 3-month timeframes.

Results
1. Baseline Demographics (n=213)

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<th>Male</th>
<th>Female</th>
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<td>74 % (158)</td>
<td>26 % (55)</td>
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Marital Status:
- Married 73 % (155)
- Never Married 11 % (23)
- Widowed/Divorced/Separated 16 % (34)

Education:
- < 10 yrs 36 % (77)
- 10 yrs 30 % (64)
- > 10 yrs 34 % (72)

Resident of:
- Bangalore City 61 % (130)
- Karnataka (outside Bangalore) 30 % (63)
- Other 9 % (20)

Age (years): mean (range) 39 (22 – 75)

Conclusions
• Self-reported adherence and virologic failure are inversely and significantly associated in this study.
• Delays in prescription refills lead to treatment interruptions and are the most common form of non-adherence and are associated with virologic failure.
• More than a quarter of the study patients were in virologic failure and among these patients, only 20% had wild-type virus. This severely limits the utility of first-line HAART in this setting.
• The severity and pattern of RTI mutations in this study shows that options for future second line therapy will be limited.
• Due to its cost, viral load is not currently part of standard HIV clinical practice in India, thus patients may be in virologic failure for months, before their clinical failure is detected by their physicians.
• The results of this study can assist in the development of national antiretroviral treatment programs for patients who experience treatment failure in resource-limited settings in which genotypic resistance testing is not readily available.
• Given the prevalence and significance of these mutations, there is an urgent need for the introduction of second line HAART in India.

References:

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